

**CRYSTAL STRUCTURE OF HUMAN INTERLEUKIN-22****EINAR NEEDS TO CHECK FIGUREs 4 and 6**

This application claims priority to provisional application no. 60/317,937 filed September 10, 2001 and provisional application no. 60/333,150 filed November 27, 2001 both incorporated herein by reference in their entirety.

**FIELD OF THE INVENTION**

The present invention relates to the fields of molecular biology, protein purification, protein crystallization, X-ray diffraction analysis, three-dimensional-structure determination, rational drug design and molecular modeling of related proteins and mutants. The present invention provides crystallization methods and crystallized human interleukin-22 (IL-22). The crystallized IL-22 is physically analyzed by X-ray diffraction techniques. The resulting X-ray diffraction patterns are of sufficiently high resolution to be useful for determining the three-dimensional structure of IL-22, molecular modeling of related proteins and mutants.

**BACKGROUND AND PRIOR ART****1. Interleukins.**

The last decade has seen knowledge of the immune system and its regulation expand tremendously. One area of particular research interest has focused on the regulatory proteins and glycoproteins of the immune system. One of the best known families of these regulatory molecules is the cytokines. These are molecules which are involved in the "communication" of cells with each other. The individual members of the cytokine family have been found to be involved in a wide variety of pathological conditions, such as cancer and allergies. Whereas sometimes the cytokines are involved in the pathology of the condition, they are also known as being therapeutically useful.

Interleukins are one type of cytokines. The literature on interleukins is vast. An exemplary, but by no means exhaustive listing of the patents in this area includes U.S.

Patent No. 4,778,879 to Mertelsmann *et al.*; U.S. Patent No. 4,490,289 to Stern; U.S. Patent No. 4,518,584 to Mark *et al.*; and U.S. Patent No. 4,851,512 to Miyaji *et al.*, all of which involve interleukin-2 or "IL-2." Additional patents have issued which relate to interleukin-1 ("IL-1"), such as U.S. Patent No. 4,808,611 to Cosman. The disclosure of all of these patents are incorporated by reference herein. More recent patents on different interleukins include U.S. Patent Nos. 5,694,234 (IL-13); 5,650,492 (IL-12); 5,700,664, 5,371,193 and 5,215,895 (IL-11); 5,728,377, 5,710,251, 5,328,989 (IL-10); 5,580,753, 5,587,302, 5,157,112, 5,208,218 (IL-9); 5,194,375, 4,965,195 (IL-7); 5,723,120, 5,178,856 (IL-6), and 5,017,691 (IL-4). Even a cursory review of this patent literature shows the diversity of the properties of the members of the interleukin family. One can assume that the larger cytokines family shows even more diversity. *See, e.g.*, Aggarwal *et al.*, ed., Human Cytokines: Handbook For Basic And Clinical Research (Blackwell Scientific Publications, 1992); Paul, ed., Fundamental Immunology (Raven Press, 1993), pp. 763-836. All cited references are incorporated by reference herein.

## 2. Interleukin-9.

The lymphokine IL-9, previously referred to as "P40," is a T-cell derived molecule which was originally identified as a factor that sustained permanent antigen independent growth of T4 cell lines. *See, e.g.*, Uyttenhove *et al.* (1988) *Proc. Natl. Acad. Sci. USA* **85**: 6934; Van Snick *et al.* (1989) *J. Exp. Med.* **169**: 363; Simpson *et al.* (1989) *Eur. J. Biochem.* **183**: 715; all of which are incorporated herein by reference.

IL-9 activity was at first observed on T4-restricted cell lines. IL-9 does not, however, show activity on CTLs or freshly isolated T cells. *See, e.g.*, Uyttenhove *et al.*, *supra*, Schmitt *et al.* (1989) *Eur. J. Immunol.* **19**: 2167. Subsequent experiments demonstrated that T-cell-growth factor III (TCGF III) is identical to mast cell growth enhancing activity (MEA), a factor that potentiates the proliferative response of bone-marrow-derived mast cells to IL-3. Studies on IL-9 have shown that it also supports erythroid colony formation (Donahue *et al.* (1990) *Blood* **75**(12): 2271-2275); promotes the proliferation of myeloid erythroid burst formation (Williams *et al.* (1990) *Blood* **76**: 306-311); supports clonal maturation of burst-forming-unit-erythrocytes (BFU-E) of

adult and fetal origin (Holbrook *et al.* (1991) *Blood* **77**(10): 2129-2134); and stimulates proliferation of megakaryoblastic leukemia cells (Yang *et al.* (1989) *Blood* **74**: 1880). IL-9 expression has also been implicated in Hodgkin's disease and large cell anaplastic lymphoma (Merz *et al.* (1990) *Blood* **78**(8): 1311-1317). Genetic analyses of mice susceptible or resistant to the development of bronchial hyperresponsiveness have linked the IL-9 gene and its expression to bronchial hyperresponsiveness susceptibility. *See, e.g.*, Nicolaides *et al.* (1997) *Proc. Natl. Acad. Sci. USA* **94**: 13175-13180. Studies with IL-9-transgenic mice demonstrate that increased IL-9 expression produces lung mastocytosis, hypereosinophilia, bronchial hyperresponsiveness and high levels of IgE. *See, e.g.*, Temann *et al.*, *J. Exp. Med.* **188**: 1307-1320, 1998; Godfraind *et al.* (1998) *J. Immunol.* **160**: 3989-3996; McLane *et al.* (1999) *Am. J. Resp. Cell. Mol.* **19**: 713-720. Genetic studies in humans have also linked IL-9 and IL-9R genes to asthma. *See, e.g.*, Doull *et al.* (1996) *Am. J. Respir. Crit. Care Med.* **153**: 1280-1284; Holroyd *et al.* (1998) *Genomics* **52**: 233-235, 1998. In combination, these observations strongly suggest that IL-9 plays a major role in bronchial hyperresponsiveness, asthma and allergies. *See, e.g.*, PCT Application US96/12757 (Levitt, *et al.*), and PCT Application US97/21992 (Levitt, *et al.*), both of which are incorporated herein by reference.

IL-9 is known to affect the levels of other molecules in subjects. *See e.g.*, Louahed *et al.* 1995) *J. Immunol.* **154**: 5061-5070; Demoulin *et al.* (1996) *Mol. Cell. Biol.* **16**: 4710-4716; both of which are incorporated herein by reference. It will be recognized that the molecules affected have their own functions in biological systems. For example, many of the known activities of IL-9 are mediated by activation of STAT transcription factors. *See e.g.*, Louahed *et al.* (1995) *J. Immunol.* **154**: 5061-5070; Demoulin *et al.* (1996) *Mol. Cell. Biol.* **16**: 4710-4716; both of which are incorporated herein by reference. As such, there is continued interest in trying to identify molecules whose presence and/or level is affected by other molecules, such as cytokines.

### 3. Interleukin-22

Interleukin-22 (IL-22) is a cytokine that is induced by IL-9 in T cells and mast cells. *See, e.g.*, Dumoutier *et al.* (2000) *J. Immunol.* **164**: 1814-1819; WO 00/24758 and

U.S. Application Serial No. 09/419,568, which are all incorporated herein by reference. The induction of IL-22 expression by IL-9 is rapid—within 1 hour. IL-22 is a 20 kDa protein that has an N-terminal hydrophobic signal peptide and shares amino-acid-sequence homology to interleukin-10 (IL-10). In addition, IL-22 binds two receptors that are members of the class-II-cytokine-receptor family. *See, e.g., Xie et al. (2000) J. Biol. Chem. 275: 31335-31339; Kotenko et al. (2001) J. Biol. Chem. 276: 2725-2732.* Recent results demonstrate that the functional IL-22 receptor complex consists of two receptor chains, the CRF2-9 (IL22R) chain and the CRF2-4 (IL-10R2 or IL-10R $\beta$ ) chain. *See, e.g., Xie et al. (2000) J. Biol. Chem. 275: 31335-31339; Kotenko et al. (2001) J. Biol. Chem. 276: 2725-2732.* Interestingly, CRF2-4, which binds an IL-10 homodimer, is a functional component of the IL-10 signaling complex. *See, e.g., Temann, et al. (1998) J. Exp. Med. 188: 1307-1320.* Although this is the first example of the involvement of a class-II-cytokine-receptor in multiple distinct cytokine signaling complexes, sharing of the gamma-common chain is observed in IL-2, IL-4, IL-7, IL-9 and IL-15 receptor complexes. Other members of the class-II-receptor family include the two interferon- $\gamma$  (IFN- $\gamma$ ) receptor chains (R $\alpha$  and R $\beta$ ), the two chains of the IFN- $\alpha/\beta$  receptor, and tissue factor. In contrast, the growth hormone (GH) and prolactin receptors, for example, are members of the class-I-cytokine-receptor family.

Human and mouse IL-22 (IL-22 and mIL-22, respectively) comprise 179 amino-acid residues, including four cysteine residues, and share about 79% sequence identity. In contrast, IL-22 shares only 25% sequence identity with human IL-10 (hIL-10), and mIL-22 shares only 22% sequence identity with hIL-10. The regions of highest sequence identity are located in the C-terminal half of IL-22 and hIL-10. The fact that this region is critical for IL-10 activity, suggests that IL-22 and IL-10 share common or related biological activities.

Although IL-22 appears to play a critical role in immune function, *in vivo* studies in mice have demonstrated that lipopolysaccharide (LPS) induces the expression of IL-22 in numerous organs. *See, e.g., Dumoutier et al. (2000) Proc. Natl. Acad. Sci. U.S.A. 97: 10144-10149.* IL-22 also activates signal transducer and activator of transcription factors (STAT), specifically STAT-1 and STAT-3, in several hepatoma cell lines. The stimulation of HepG2-human-hepatoma cells up-regulates the production of acute-phase

reactants such as serum amyloid A,  $\alpha$ -1-antichymotrypsin and haptoglobin. *See, e.g.,* Dumoutier *et al.* (2000) *Proc. Natl. Acad. Sci. U.S.A.* **97**: 10144-10149. A similar induction of acute-phase reactants was observed upon injection of IL-22 into mouse liver. These findings suggest that IL-22 plays a role in the inflammatory response. Importantly, the IL-22 gene is located on human chromosome 12q near a cluster of genetic loci linked to asthma. *See, e.g.,* Xie *et al.* (2000) *J. Biol. Chem.* **275**: 31335-31339; Kotenko, *et al.* (2001) *J. Biol. Chem.* **276**: 2725-2732. Thus, these findings, the induction of IL-22 by IL-9, and the association of IL-9 with inflammation and airway hyperreactivity disorders, in combination, implicate IL-22 in the etiology of asthma and allergy.

The present invention discloses a refined three-dimensional structure of IL-22 of sufficient resolution to identify the IL-22 dimerization interface and the specific amino acid residues that are involved in stabilizing the IL-22 dimer. Although both IL-10 and IL-22 form dimers, and IL-10 binds its receptor as a dimer, the present invention demonstrates that IL-22 binds the IL-22 receptor as a monomer. The present invention provides mutant IL-22 wherein the mutation or mutations destabilize the dimer. These IL-22 mutants provide IL-22 in its biologically active form and are useful as therapeutic agents. The three-dimensional structure of IL-22 of the present invention is also of sufficient resolution to allow the identification of the specific amino acids involved in binding the IL-22 receptor. In addition the present invention provides mutant IL-22 wherein the mutation(s) modify the ability of the mutant IL-22 to bind its receptor. Human IL-22 mutants with increased affinity for the IL-22 receptor are therapeutically useful agonists and antagonists. Furthermore, the present invention provides a crystal structure of sufficient quality for use in methods of rational drug design to produce therapeutically relevant molecules.

## SUMMARY OF THE INVENTION

The present invention provides methods for identifying a mammalian IL-22 mutant with modified ability to dimerize, said method comprising the steps of: (a) constructing a three-dimensional structure of IL-22 defined by the atomic coordinates shown in Table 4; (b) employing the three-dimensional structure and modeling methods

to identify an amino acid involved in stabilizing a dimer of IL-22; (c) producing a mammalian IL-22 having a mutation at an amino acid identified in (b); and (d) assaying said mutant IL-22 to determine the ability of said mutant to dimerize as compared to an IL-22 control, wherein a difference in dimerization between said mutant and said control is indicative of a modified ability to dimerize. As used herein, “IL-22”, “T-cell-inducible factor (TIF)” and “IL-TIF/IL-22” each refer to a cytokine of about 20 kDa that has an N-terminal hydrophobic signal peptide amino acid sequence homology to interleukin 10 (IL-10), and is upregulated by interleukin-9 (IL-9) in T cells and mast cells. *See, e.g.,* Dumoutier *et al.* (2000) *J. Immunol.* **164**: 1814-1819. As used herein, “mammalian IL-22” or “IL-22” refers to a mammalian cytokine of about 20 kDa, which has an N-terminal hydrophobic signal peptide, amino acid sequence homology to interleukin 10 (IL-10), and is upregulated by interleukin-9 (IL-9) in T cells and mast cells. Preferably, mammalian IL-22 is from, for example, human, horses, cows, sheep, goats, cats, dogs, pigs, rats and mice. More preferably, mammalian IL-22 is human IL-22 (IL-22). In a preferred embodiment, “human IL-22” consists of the amino acid sequence of SEQ ID NO: 2.

As used herein, “ability to dimerize” refers to the ability of two IL-22 monomers to form an IL-22 dimer. Mutations that either strengthen inter-monomer contacts or weaken the inter-monomer interactions modify the ability of IL-22 to dimerize. As used herein, “stabilizing the dimer” refers to the effect of an energetically favorable mutation that strengthens inter-monomer contacts. As used herein, an amino acid is “involved” in stabilizing the dimer when the amino acid directly or indirectly contributes to the stability of the dimer—either sterically or through non-covalent bonding (*i.e.* van der Waals interactions, hydrogen bonding, hydrophobic interactions, etc.), and the like. As used herein, “mutation site” refers to a single amino acid of an IL-22. The IL-22 mutant, however, includes IL-22 molecules that contain mutations at one or more mutation sites. As used herein, “mutation” or “mutations” refers to a substitution of one or more amino acids; a deletion of one or more amino acids; or the addition of one or more amino acids. Preferably, a mutation of the present invention is the substitution, deletion or addition of a single amino acid at one or more mutation sites.

In a preferred embodiment, the “mutation site”, that is identified by the three-dimensional structure of IL-22 and modeling methods of the present invention, is an amino acid at a position that is at or near the dimerization interface. More preferably, the “mutation site” is one or more amino acids that are located at the dimerization interface. As used herein, “dimerization interface” refers to the contact area between the two monomers of a dimer. In a preferred embodiment, the contact area between the two monomers of a dimer include amino acid positions 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, at least two of these amino acid positions or all of these amino acid positions of SEQ ID NO: 2. More preferably, the dimerization interface comprises amino acids at positions corresponding to positions 44, 48, 49, 57, 61, 64, 73, 75, 83, 166, 168, 175, 176, or 179 of SEQ ID NO: 2, at least two of these amino acid positions, or all of these amino acid positions.

The present invention also provides an isolated peptide selected from the group consisting of:

- (a) an amino acid sequence consisting essentially of amino acids 61-71 of SEQ ID NO: 2;
- (b) an amino acid sequence consisting essentially of amino acids 61-162 of SEQ ID NO: 2;
- (c) an amino acid sequence consisting essentially of amino acids 61-169 of SEQ ID NO: 2;
- (d) an amino acid sequence consisting essentially of amino acids 162-169 of SEQ ID NO: 2;
- (e) an amino acid sequence consisting essentially of amino acids 98-104 of SEQ ID NO: 2; and
- (f) an amino acid sequence consisting essentially of amino acids 98-157 of SEQ ID NO: 2.

In a preferred embodiment the amino acid sequence of the isolated peptide contains a mutation at one or more positions corresponding to position 61, 70, 71, 98-104, 154-157, 162, 166, and 169 of SEQ ID NO: 2.

Another embodiment of the present invention provides mimetics of peptides corresponding to Region 1 or Region 2, mimetics of fragments of peptides corresponding to Region 1 or Region 2 that bind an IL-22 receptor or an IL-22 receptor chain CRF2-4 and/or CRF2-9 or mutants of peptides corresponding to Region 1 or Region 2 and/or mutants thereof.

The mimetics of the present invention includes peptide-containing molecules that mimic elements of protein secondary structure. See e.g., Johnson *et al.*, In: Biotechnology And Pharmacy (Pezzuto *et al.*, eds.; Chapman and Hall, New York, (1993); Coligan *et al.* (1991) *Current Protocols in Immunology* 1(2): Chapter 5; both incorporated by reference herein. The underlying rationale behind the use of peptide mimetics is that the peptide backbone of proteins exists chiefly to orient amino acid side chains in such a way as to facilitate molecular interactions, such as those of antibody and antigen or receptor and ligand. A peptide mimetic permits molecular interactions similar to the natural molecule. These principles may be used, in conjunction with the principles outline above, to engineer second generation molecules having IL-22-receptor-binding properties that are improved as compared to unmodified IL-22.

As used herein, the terms "peptidomimetic" and "mimetic" is intended to include peptide analogues which serve as appropriate substitutes for peptides in interactions with, for example, receptors. The peptidomimetic must possess not only affinity, but also efficacy and substrate function. That is, a peptidomimetic exhibits functions of a peptide, without restriction of structure to amino acid constituents. Peptidomimetics, methods for their preparation and use are described in Morgan *et al.* (1989). See e. g., Morgan *et al.* In: Ann. Rep. Med. Chem. (Virick F. J., *et al.*, eds.; Academic Press, San Diego, Calif., 1989) pp. 243-253; incorporated by reference herein. Peptidomimetics and the mutant polypeptides of the present invention may also include targeting moieties or molecules that direct the mimetics and polypeptides to specific tissues and cells. Many targeting moieties are known, and include, for example, asialoglycoproteins (See e.g., U.S. Pat. No. 5,166,320 to Wu) and other ligands which are transported into cells via receptor-mediated endocytosis.



Peptide combinatorial libraries are particularly useful for identifying the mimetics of the present invention (Simon *et al.* (1992) *Proc. Natl. Acad. Sci. USA* **89**: 9367; incorporated herein by reference) and can be used to generate chemically diverse libraries of novel molecules. Once the peptide libraries are generated, they can be screened, for example, by using antibodies—polyclonal or monoclonal antibodies—that are specific to the mutant peptides corresponding to Region 1 and Region 2 of an IL-22, or mutant peptides of the present invention. These antibodies may be added to mimetics derived from the peptide libraries. After a period of incubation and a wash to remove unbound antibody, the presence of bound antibody is determined by standard ELISA assays. *See, e.g.*, Harlow & Lane Antibodies: A Laboratory Manual (Cold Spring Harbor Laboratory; Cold Spring Harbor, N.Y., 1988) pg. 553. Wells that do not contain bound antibody indicate the presence of peptide mimetics that bind to the antibody. Methods for identifying active compounds in pools of small molecules include fractionating the pool by reverse phase HPLC or affinity selection/mass spectroscopy. *See, e.g.*, Nedved *et al.* (1996) *Anal. Chem.* **68**: 4228; Zuckermann *et al.* (1994) *J. Med. Chem.* **37**: 2678; both incorporated herein by reference.

As used herein, the term “mimetic”, is not limited to peptide-based mimetics or peptidomimetics. As used herein, the term “mimetics”, refers to any molecule capable of mimicking IL-22 and the biological properties of IL-22 (*i.e.*, binding activity and/or inducing a receptor-mediated downstream biological effect characteristic of IL-22). The mimetics of the present invention may be a protein, peptide, or non-peptidyl based organic molecule. Accordingly, the term “mimetic” embraces any substance having IL-22-like activity, regardless of the chemical or biochemical nature thereof. The mimetics of the present invention may be a simple or complex substance produced by a living system or through chemical or biochemical synthetic techniques. A mimetic of the present invention can be a large molecule, *e.g.*, a mutant IL-22 dimer or monomer, as described herein, or a small molecule, *e.g.*, an organic molecule prepared *de novo* according to the principles of rational drug design. The mimetics of the present invention that are based on mutants of IL-22 also include any substance that structurally resembles a solvent-exposed surface epitope of IL-22 and binds an IL-22 receptor or IL-22 receptor chains. Methods of modeling, identifying and producing the mimetics of the

present invention are disclosed in U. S. Patent Nos. 5,835,382; 6,090,609; 6,242,201; 6,251,620; 6,273,598; and 6,303,287; all incorporated herein by reference.

The present invention also provides methods for identifying and producing mimetics of an IL-22 receptor or IL-22 receptor chain comprising the steps of: a) constructing a three-dimensional structure of hIL-22 defined by the atomic coordinates shown in Table 4; b) employing the three-dimensional structure and modeling methods to identify one or more surface accessible amino acids or one or more amino acids involved in receptor binding; c) producing a mimetic that binds or interacts with the IL-22 at one or more amino acids identified in (b); and c) assaying said mimetic to determine the ability of said mimetic to prevent or reduce the binding of IL-22 to an IL-22 receptor or receptor chain as compared o an IL-22 control, wherein a difference in IL-22 binding between said mimetic and said control is indicative of an IL-22 receptor or IL-22 receptor chain mimetic. In a preferred embodiment, the surface accessible amino acids comprise one or more amino acids selected from the group consisting the amino acids listed in Table 5. In another embodiment, the one or more amino acids involved in IL-22 receptor or IL-22 receptor chain binding are preferably the amino acids comprising Region 1 and/or Region 2. More preferably, the one or more amino acids involved in IL-22 receptor or IL-22 receptor chain binding are selected from the group consisting of the amino acid at a position corresponding to position 61, 70, 71, 162, 166, 169, 98, 99, 100, 101, 102, 103, 104, 154, 155, 156 and 157 of SEQ ID NO: 2.

The present invention also provides a mimetic of an IL-22 receptor or IL-22 receptor chain that is produced by a method comprising the steps of: a) constructing a three-dimensional structure of hIL-22 defined by the atomic coordinates shown in Table 4; b) employing the three-dimensional structure and modeling methods to identify one or more surface accessible amino acids or one or more amino acids involved in receptor binding; c) producing a mimetic that binds or interacts with the IL-22 at one or more amino acids identified in (b); and c) assaying said mimetic to determine the ability of said mimetic to prevent or reduce the binding of IL-22 to an IL-22 receptor or receptor chain as compared o an IL-22 control, wherein a difference in IL-22 binding between said mimetic and said control is indicative of an IL-22 receptor or IL-22 receptor chain mimetic. In a preferred embodiment, the surface accessible amino acids comprise one or

more amino acids selected from the group consisting the amino acids listed in Table 5. In another embodiment, the one or more amino acids involved in IL-22 receptor or IL-22 receptor chain binding are preferably the amino acids comprising Region 1 and/or Region 2. More preferably, the one or more amino acids involved in IL-22 receptor or IL-22 receptor chain binding are selected from the group consisting of the amino acid at a position corresponding to position 61, 70, 71, 162, 166, 169, 98, 99, 100, 101, 102, 103, 104, 154, 155, 156 and 157 of SEQ ID NO: 2.

The present invention also provides antibodies or fragments thereof that specifically bind to one or more epitopes in a region comprising an IL-22 dimerization interface and/or a region involved in IL-22 receptor or IL-22 receptor chain binding. In a preferred embodiment, the antibodies of the present invention are polyclonal antibodies. In a more preferred embodiment, the antibodies of the present invention are monoclonal antibodies. The antibodies of the present invention bind one or more epitopes in a region comprising an IL-22 dimerization interface and/or a region involved in IL-22 receptor or IL-22 receptor chain binding and preferably prevent or interfere with the formation of IL-22 dimers and/or prevent or interfere with the binding of IL-22 to an IL-22 receptor or IL-22 receptor chain, respectively. In a preferred embodiment, the one or more epitopes are located in a region comprising the IL-22 dimerization interface. In a more preferred embodiment, the one or more epitopes comprise one or more of the amino acids selected from the group consisting of amino acids corresponding to positions 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, or 179 of SEQ ID NO: 2. In a most preferred embodiment, the one or more epitopes comprise one or more of the amino acids selected from the group consisting of amino acids corresponding to positions 44, 48, 49, 57, 61, 64, 73, 75, 83, 166, 168, 175, 176, or 179 of SEQ ID NO: 2. In a preferred embodiment, the one or more epitopes are located in a region comprising the IL-22 receptor- or IL-22-receptor-chain-binding domains. In a more preferred embodiment, the one or more epitopes are located in Region 1 and/or Region 2. In a most preferred embodiment, the epitopes in Region 1 comprise one or more of the amino acids at positions corresponding to positions 61, 70, 71, 162, 166, and 169 of SEQ ID

NO: 2. In a most preferred embodiment, the epitopes in Region 2 comprise one or more of the amino acids at positions corresponding to positions 98, 99, 100, 101, 102, 103, 104 154, 155, 156, or 157 of SEQ ID NO: 2.

The present invention also provides methods for identifying a mutant of a mammalian IL-22 with modified ability to bind an IL-22 receptor, said method comprising the steps of: (a) constructing a three-dimensional structure of IL-22 defined by the atomic coordinates shown in Table 4; (b) employing the three-dimensional structure and modeling methods to identify an amino acid involved in receptor binding; (c) producing any IL-22 having a mutation at an amino acid identified in (b); and (d) assaying said mutant IL-22 to determine the ability of said mutant to bind to the IL-22 receptor as compared to an IL-22 control, wherein a difference in binding between said mutant and said IL-22 control is indicative of a modified ability to bind the IL-22 receptor. As used herein, "IL-22 control" refers to an unmodified mammalian IL-22 that is identical to the mutant IL-22 prior to incorporation of the mutation.

In a preferred embodiment, the mutation site is located in an IL-22-receptor-binding site. More preferably, the IL-22-receptor-binding site is Region 1 or Region 2. As used herein, "Region 1" refers to the region of IL-22 that is formed by helix A, loop AB and helix F and binds to the IL-22-receptor chain, CRF2-4 and/or CRF2-9. As used herein, "Region 2" refers to the region of IL-22 that is formed by helix C and helix E and binds to the IL-22-receptor chain, CRF2-4. In a more preferred embodiment, the mutation site in Region 1 is selected from one or more of the amino acids at positions corresponding to positions 61, 70, 71, 162, 166, and 169 of SEQ ID NO: 2. In another embodiment, the mutation in site in Region 2 is selected from at least one of the amino acids at positions corresponding to positions 98, 99, 100, 101, 102, 103, 104 154, 155, 156, or 157 of SEQ ID NO: 2.

The present invention also provides a mutant IL-22 comprising at least one amino acid substitution in Region 1 or Region 2 or a combination thereof. More preferably, the mutant IL-22 comprises a mutation in Region 1 at one or more positions corresponding to position 44, 48, 49, 57, 61, 64, 73, 75, 83, 166, 168, 175, 176, and 179 of SEQ ID NO: 2, and/or a mutation in Region 2 at one or more positions corresponding to positions 98,

99, 100, 101, 102, 103, 104, 154, 155, 156, or 157 of SEQ ID NO: 2. The present invention also contemplates mutant IL-22 molecules that comprise Region 1, wherein the mutant IL-22 comprises a mutation at one or more positions corresponding to position 44, 48, 49, 57, 61, 64, 73, 75, 83, 166, 168, 175, 176, or 179 of SEQ ID NO: 2, and/or a mutant IL-22 molecule that comprises Region 2, wherein the mutant IL-22 comprises a mutation at one or more positions corresponding to position 98, 99, 100, 101, 102, 103, 104, 154, 155, 156, or 157 of SEQ ID NO: 2.

The present invention also provides a mutant IL-22 comprising at least one amino acid substitution at an IL-22 dimerization interface. Preferably, the dimerization interface comprises amino acids at positions corresponding to positions 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 5, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, or 179 of SEQ ID NO: 2. More preferably, the dimerization interface comprises amino acids at positions corresponding to positions 44, 48, 49, 57, 61, 64, 73, 75, 83, 166, 168, 175, 176, or 179 of SEQ ID NO: 2.

In another embodiment, the present invention provides a mutant IL-22 comprising at least one amino acid substitution at a IL-22 dimerization interface, wherein the mutation(s) are at a position or positions that stabilize an IL-22 dimer. Preferably, the mutation or mutations are selected from one or more of the group consisting of:

- (a) an amino acid at a position corresponding to position 166 or 175 of SEQ ID NO: 2;
- (b) an amino acid at a position corresponding to position 57 or 176 of SEQ ID NO: 2;
- (c) an amino acid at a position corresponding to position 73 or 83 of SEQ ID NO: 2;
- (d) an amino acid at a position corresponding to position 44 or 64 of SEQ ID NO: 2;
- (e) an amino acid at a position corresponding to position 168 or 175 of SEQ ID NO: 2;

(f) an amino acid at a position corresponding to position 75 or 176 of SEQ ID NO: 2;

(g) an amino acid at a position corresponding to position 48 or 61 of SEQ ID NO: 2;

(h) an amino acid at a position corresponding to position 44 or 166 of SEQ ID NO: 2;

(i) an amino acid at a position corresponding to position 61 or 179 of SEQ ID NO: 2; and

(j) an amino acid at a position corresponding to position 49 or 61 of SEQ ID NO: 2.

More preferably, the mutation is at one or more amino acid positions corresponding to position 175 of SEQ ID NO: 2, wherein the substitution is any amino acid except arginine and lysine; position 166 of SEQ ID NO: 2, wherein the substitution is any amino acid except glutamate, aspartate, glutamine, asparagine, serine, threonine and cysteine; position 176 of SEQ ID NO: 2, wherein the substitution is any amino acid except arginine, lysine, asparagine and glutamine; position 73 of SEQ ID NO: 2, wherein the substitution is any amino acid except arginine and lysine; position 44 of SEQ ID NO: 2, wherein the substitution is any amino acid except arginine and lysine; position 64 of SEQ ID NO: 2, wherein the substitution is any amino acid except glutamate, aspartate, glutamine, asparagine, serine, threonine and cysteine; position 168 of SEQ ID NO: 2; wherein the substitution is any amino acid except glutamate, aspartate, glutamine, asparagine, serine, threonine and cysteine; position 61 of SEQ ID NO: 2, wherein the substitution is any amino acid except arginine and lysine; position 166 of SEQ ID NO: 2, wherein the substitution is any amino acid except glutamate, aspartate, glutamate, glutamine, asparagine, serine, threonine and cysteine; and position 49 of SEQ ID NO: 2, wherein the substitution is any amino acid except glutamine, asparagine, glutamate and aspartate.

The present invention also provides isolated polynucleotides that encode a mutant IL-22 comprising at least one amino acid substitution in Region 1 or Region 2. More preferably, the polynucleotides encode the mutant IL-22 that comprises a mutation in Region 1 at one or more positions corresponding to position 44, 48, 49, 57, 61, 64, 73, 75, 83, 166, 168, 175, 176, and 179 of SEQ ID NO: 2, and/or a mutation in Region 2 at

one or more positions corresponding to positions 98, 99, 100, 101, 102, 103, 104, 154, 155, 156, or 157 of SEQ ID NO: 2. The present invention also contemplates polynucleotides that encode mutant IL-22 molecules that comprise Region 1, wherein the mutant IL-22 comprises at least one mutation at a position corresponding to position 44, 48, 49, 57, 61, 64, 73, 75, 83, 166, 168, 175, 176, or 179 of SEQ ID NO: 2, and/or a mutant IL-22 molecule that comprises Region 2, wherein the mutant IL-22 comprises at least one mutation at a position corresponding to position 98, 99, 100, 101, 102, 103, 104, 154, 155, 156, or 157 of SEQ ID NO: 2.

In another embodiment, the isolated polynucleotides encode mutant IL-22 comprising at least one amino acid substitution at a IL-22 dimerization interface. Preferably, the dimerization interface comprises amino acids at positions corresponding to positions 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, or 179 of SEQ ID NO: 2. More preferably, the dimerization interface comprises amino acids at positions corresponding to positions 44, 48, 49, 57, 61, 64, 73, 75, 83, 166, 168, 175, 176, or 179 of SEQ ID NO: 2.

In another embodiment, the present invention provides isolated polynucleotides that encode a mutant IL-22 comprising at least one amino acid substitution at an IL-22 dimerization interface, wherein the mutation or mutations are at a position or positions that stabilize an IL-22 dimer. Preferably, the mutation or mutations are selected from one of more of the group consisting of:

- (a) an amino acid at a position corresponding to position 166 or 175 of SEQ ID NO: 2;
- (b) an amino acid at a position corresponding to position 57 or 176 of SEQ ID NO: 2;
- (c) an amino acid at a position corresponding to position 73 or 83 of SEQ ID NO: 2;
- (d) an amino acid at a position corresponding to position 44 or 64 of SEQ ID NO: 2;

- (e) an amino acid at a position corresponding to position 168 or 175 of SEQ ID NO: 2;
- (f) an amino acid at a position corresponding to position 75 or 176 of SEQ ID NO: 2;
- (g) an amino acid at a position corresponding to position 48 or 61 of SEQ ID NO: 2;
- (h) an amino acid at a position corresponding to position 44 or 166 of SEQ ID NO: 2;
- (i) an amino acid at a position corresponding to position 61 or 179 of SEQ ID NO: 2; and
- (j) an amino acid at a position corresponding to position 49 or 61 of SEQ ID NO: 2.

More preferably, the isolated polynucleotides encode an IL-22 mutant, wherein the mutation is at one or more amino acid positions corresponding to position 175 of SEQ ID NO: 2, wherein the substitution is any amino acid except arginine and lysine; position 166 of SEQ ID NO: 2, wherein the substitution is any amino acid except glutamate, aspartate, glutamine, asparagine, serine, threonine and cysteine; position 176 of SEQ ID NO: 2, wherein the substitution is any amino acid except arginine, lysine, asparagine and glutamine; position 73 of SEQ ID NO: 2, wherein the substitution is any amino acid except arginine and lysine; position 44 of SEQ ID NO: 2, wherein the substitution is any amino acid except arginine and lysine; position 64 of SEQ ID NO: 2, wherein the substitution is any amino acid except glutamate, aspartate, glutamine, asparagine, serine, threonine and cysteine; position 168 of SEQ ID NO: 2; wherein the substitution is any amino acid except glutamate, aspartate, glutamine, asparagine, serine, threonine and cysteine; position 61 of SEQ ID NO: 2, wherein the substitution is any amino acid except arginine and lysine; position 166 of SEQ ID NO: 2, wherein the substitution is any amino acid except glutamate, aspartate, glutamate, glutamine, asparagine, serine, threonine and cysteine; and position 49 of SEQ ID NO: 2, wherein the substitution is any amino acid except glutamine, asparagine, glutamate and aspartate.

The present invention also provides a mutant IL-22 comprising at least one amino acid substitution at one or more glycosylation sites, wherein the substitution prevents or reduces the glycosylation of IL-22. In a preferred embodiment, the at least one amino



acid substitution is at a position selected from the group consisting of amino acid positions corresponding to position 54, 55, 56, 97, 98 or 99 of SEQ ID NO: 2. In a more preferred embodiment, the at least one amino acid substitution corresponds to position 54, 56, 97, or 99 of SEQ ID NO: 2, or a combination thereof.

In another embodiment, the mutant IL-22 comprises one or more amino acid substitutions, wherein the substitution or substitutions produce a glycosylation site at the dimerization interface. In a preferred embodiment, the glycosylation site consists of the amino acid sequence Asn-Xaa-Thr/Ser. In one embodiment, insertion of a glycosylation site increases the glycosylation of IL-22. In another embodiment, insertion of a glycosylation site increases the glycosylation of IL-22 and prevents or reduces the dimerization of IL-22 as compared to an unsubstituted IL-22.

In another embodiment, a mutant IL-22 of the present invention comprising a mutation in Region 1, Region 2, or at the dimerization interface, further comprises one or more amino acid substitutions, wherein the substitution or substitutions produce a glycosylation site at the dimerization interface. In a preferred embodiment, the glycosylation site consists of the amino acid sequence Asn-Xaa-Thr/Ser. In one embodiment, insertion of a glycosylation site increases the glycosylation of IL-22. In another embodiment, insertion of a glycosylation site increases the glycosylation of IL-22 and prevents or reduces the dimerization of IL-22 as compared to an unsubstituted IL-22.

The present invention also provides a computer system comprising: a) a memory comprising atomic coordinates shown in Table 4; and b) a processor in electrical communication with the memory; wherein the processor generates a molecular model having a three dimensional shape representative of at least a portion of a mammalian IL-22. In a preferred embodiment, the atomic coordinates shown in Table 4 are stored on a computer readable diskette.

The present invention also provides cloning and expression vectors that comprise the polynucleotides of the present invention. In another embodiment, host cells are transformed with the vectors of the present invention and are used in methods of

producing the encoded mutant IL-22 that comprise culturing the host cells and isolating the mutant IL-22.

The present invention also provides pharmaceutical compositions comprising the mutant IL-22, peptides or mimetics of the present invention and a pharmaceutically acceptable carrier. As used herein, “pharmaceutically acceptable carrier” refers to any carrier, solvent, diluent, vehicle, excipient, adjuvant, additive, preservative, and the like, including any combination thereof, that is routinely used in the art.

Physiological saline solution, for example, is a preferred carrier, but other pharmaceutically acceptable carriers are also contemplated by the present invention. The primary solvent in such a carrier may be either aqueous or non-aqueous. The carrier may contain other pharmaceutically acceptable excipients for modifying or maintaining pH, osmolarity, viscosity, clarity, color, sterility, stability, rate of dissolution, and/or odor. Similarly, the carrier may contain still other pharmaceutically acceptable excipients for modifying or maintaining the stability, rate of dissolution, release, or absorption or penetration across the blood-brain barrier.

The pharmaceutical compositions of the present invention may be administered orally, topically, parenterally, rectally or by inhalation spray in dosage unit formulations that contain conventional non-toxic pharmaceutically acceptable carriers, adjuvants and vehicles. As used herein, “parenterally” refers to subcutaneous, intravenous, intramuscular, intrasternal, intrathecal, and intracerebral injection, including infusion techniques.

The pharmaceutical compositions may be administered parenterally in a sterile medium. The compositions, depending on the vehicle and concentration used, may be

suspended or dissolved in the vehicle. Advantageously, adjuvants such as local anesthetics, preservatives and buffering agents can be dissolved in the vehicle. The most preferred route of parenteral administration of the pharmaceutical compositions of the present invention is subcutaneous, intramuscular, intrathecal or intracerebral. Other embodiments of the present invention encompass administration of the composition in combination with one or more agents that promote penetration of active ingredients across the blood-brain barrier, and/or slow-release of the active ingredient(s). Such excipients include those substances usually and customarily used to formulate dosages for parenteral administration in either unit dose or multi-dose form or for direct infusion into the CSF by continuous or periodic infusion from an implanted pump.

The desired or optimal dose of the compositions of the present invention may be obtained by parenteral administration that is repeated daily, more frequently, or less frequently. The compositions may also be infused continuously or periodically from an implanted pump. The frequency of dosing will depend on the pharmacokinetic parameters of the specific mutant IL-22, peptide or mimetic in the formulation and the route of administration.

In more preferred embodiments, the pharmaceutical compositions are administered as orally active formulations, inhalant spray or suppositories. The pharmaceutical compositions of the present invention may be in a form suitable for oral use, for example, as tablets, troches, lozenges, aqueous or oily suspensions, dispersible powders or granules, emulsions, hard or soft capsules, syrups or elixirs.

Active ingredient may be combined with the carrier materials in an amount to produce a single dosage form. The amount of the active ingredient will vary, depending

upon the identity of the mutant, peptide, or mimetic, the host treated, and the particular mode of administration.

Regardless of the manner of administration, however, the specific dose is calculated according to approximate body weight or body surface area of the patient. Further refinement of the dosing calculations necessary to optimize dosing for each of the contemplated formulations is routinely conducted by those of ordinary skill in the art without undue experimentation, especially in view of the dosage information and assays disclosed herein.

The present invention also provides a method of treating a subject in need of IL-22, comprising the step of administering one of the pharmaceutical composition of the present invention, wherein the pharmaceutical composition is an IL-22-receptor agonist.

The present invention also provides a method of inhibiting IL-22 in a subject in need thereof, comprising the step of administering one of the pharmaceutical composition of the present invention, wherein the pharmaceutical composition inhibits the activation of an IL-22 receptor by IL-22.

#### BRIEF DESCRIPTION OF THE DRAWINGS

**Figure 1. (A)** Stereoview of the C $\alpha$  trace of the dimeric structure of IL-22. **(B)** Schematic representation of the secondary structure of IL-22 monomer A, according to PROCHECK (Laskowski *et al.* (1993) *J. Appl. Crystallogr.* **26**: 283-291; Polikarpov *et al.* (1997) *Nucl. Instrum. Methods* **405**: 159-164), showing the location of the two disulfide bonds (Cys40-Cys132 and Cys89-Cys178). The figures were prepared using Molscript (Dauter, *et al.* (2000) *Acta Cryst.* **D56**: 232-237), Bobscript (Nagem *et al.* (2001) *Acta Cryst.* **D57**: 996-1002) and Raster3D (Perrakis *et al.* (1999) *Nature Struct. Biol.* **6**: 458-463).

**Figure 2.** Least-square fit of monomer A to monomer B. The root-mean-square deviation (rmsd) is shown as a function of residue numbers. Only main chain atoms were used in calculation.

**Figure 3.** Contact surface of the IL-22 dimer, shaded according to residue hydrophobicity (A,B) and electrostatic potential (C,D). (A,C) show the interface of monomer A, whereas (B,D) show the interface of monomer B. In parts (A) and (B) the darker the stippled shading the greater the hydrophobicity. In parts (C) and (D) areas of negative, positive and neutral electrostatic potential are in medium stippling, dark stippling and light or no stippling, respectively. The figures were prepared with GRASP. See, e.g., Brünger, *et al.* (1998) *Acta Cryst.* **D54**: 905-921.

**Figure 4.** Secondary structure diagram showing the superposition of an IL-22 monomer (in medium stippling) onto (A) a hIL-10 dimer (from helices A to D in dark stippling and from helices E' to F' in light stippling; helices A' to D', E and F were omitted) and (B) a hIFN- $\gamma$  dimer (from helices A to D in light stippling and from helix E' to F' in black; helices A' to D', E and F were omitted). Superposition of an IL-22 dimer (in dark stippling and no stippling) onto (C) a hIL-10 dimer (in black and light stippling) and (D) a hIFN- $\gamma$  dimer (in medium stippling and light stippling).

**Figure 5.** Primary structure alignment of murine, and human IL-22 (SEQ ID NO: 3 and 2 respectively) and human IL-10 (SEQ ID NO: 1). Whenever possible, the three dimensional information was used to improve alignment. Disulfide bonds in IL-22 are marked with filled-in circles. The amino acid similarity between IL-22 and hIL-10, as calculated by the program ALSCRIPT (Nicholls *et al.* (1991) *Struct. Funct. Genet.* 11: 281-296), are boxed. Residues conserved in mIL-22 and IL-22 are boxed in the sequence of mIL-22. The loops and helices of human IL-22's secondary structure are depicted. The figure was drawn using the program ALSCRIPT (Nicholls *et al.* (1991) *Struct. Funct. Genet.* 11: 281-296).

**Figure 6.** (A) Superposition of the hIFN- $\gamma$ /hIFN- $\gamma$ R $\alpha$  complex (hIFN- $\gamma$  light stippling and medium stippling; hIFN- $\gamma$ R $\alpha$  normal) onto IL-22 monomer (dark stippling). Superposition of (B) hIFN- $\gamma$  (light stippling and darkest stippling) and (C)

hIL-10 (darkest stippling and light stippling) onto IL-22 in a coil representation of the potential receptor binding site of IL-22 (medium stippling). Residues involved in direct interaction with a receptor chain are also shown.

## DETAILED DESCRIPTION OF THE INVENTION

The present invention provides methods for crystallizing human interleukin-22. The resultant crystals diffract X-rays with sufficiently high resolution to allow determination of the atomic coordinates and solve the three-dimensional structure of IL-22. The three-dimensional structure, as provided on computer-readable media described herein, is useful for rational drug design of IL-22-related mimetics, IL-22 mutants and ligands of the IL-22 receptor. Such mimetics, mutants and ligands are useful for treating and inhibiting IL-22-mediated processes or IL-22-related disorders and diseases such as asthma, inflammation and cancer.

### 1. IL-22 Crystallization.

The isolation and purification of human IL-22, including polynucleotides, vectors and transformed or transfected host cells encoding IL-22, and recombinant methods of IL-22 production, are described in WO 00/24758 and U.S. Application Serial No. 09/419,568, which are both incorporated herein in their entirety. The amino acid sequences of mouse IL-22, human IL-22 and human IL-10 are presented in Figure 5 as SEQ ID NO: 3, 2, and 1, respectively.

Recombinant IL-22 of the present invention may be produced by the following process or other recombinant protein expression methods:

- a. constructing, by conventional molecular-biology methods, an expression vector comprising an operon that encodes IL-22, thereby producing a vector for the expression of IL-22;
- b. transferring the expression vectors to a host cell by conventional molecular biology methods to produce a transfected or transformed host cell for the expression of IL-22; and



used. Notably, the choice of expression vector is dependent upon the choice of host cell, and may be selected so as to have the desired expression and regulatory characteristics in the selected host cell.

The first prerequisite for solving the three-dimensional structure of a protein by X-ray crystallography is a well-ordered crystal that will strongly diffract X-rays. X-rays are directed onto a regular, repeating array of identical molecules so that the X-rays are diffracted from it in a pattern from which the structure of an individual molecule can be retrieved. Different crystal forms can be more or less well-ordered and hence give diffraction patterns of different quality. As a general rule, the more closely the protein molecules pack, and consequently the less water the crystals contain, the better is the diffraction pattern because the molecules are better ordered in the crystal. Well-ordered crystals of globular protein molecules are large, spherical, or ellipsoidal objects with irregular surfaces, and crystals thereof contain large holes or channels that are formed between the individual molecules. These channels, which usually occupy more than half the volume of the crystal, are filled with disordered solvent molecules. The protein molecules are in contact with each other at only a few small regions. This is one reason why structures of proteins determined by X-ray crystallography are generally the same as those for the proteins in solution.

The formation of crystals is dependent on a number of different parameters, including pH, temperature, protein, concentration, the nature of the solvent and precipitant, as well as the presence of added ions or ligands. Crystallization experiments may be needed to screen all these parameters for the few combinations that might give crystals suitable for X-ray diffraction analysis. Crystallization robots can automate and speed up the work of reproducibly setting up large number of crystallization experiments.

A pure and homogeneous protein sample is important for successful crystallization. Proteins obtained from cloned genes in efficient expression vectors can quickly be purified to homogeneity in large quantities in a few purification steps. A protein to be crystallized is preferably at least 93-99% pure, according to standard criteria of homogeneity. Crystals form when molecules are precipitated very slowly from



supersaturated solutions. The most frequently used procedure for making protein crystals is the hanging-drop method, in which a drop of protein solution is brought very gradually to supersaturation by loss of water from the droplet to the larger reservoir that contains salt or polyethylene glycol solution.

In general, IL-22 is purified as described in WO 00/24758 and U.S. Application Serial No. 09/419,568, which are both incorporated herein by reference. The resulting IL-22 is in sufficiently pure and concentrated for crystallization. The purified IL-22 preferably runs as a single band under reducing or nonreducing polyacrylamide gel electrophoresis (PAGE) (nonreducing conditions are used to evaluate the presence of disulfide bonds). Purified IL-22 is preferably crystallized using the hanging drop method under varying conditions of at least one of the following: pH, buffer type, buffer concentration, salt type, polymer type, polymer concentration, other precipitating agents and concentration of purified and cleaved IL-22. *See, e.g.*, the methods provided in a commercial kit, such as CRYSTAL SCREEN (Hampton Research, Riverside, Calif.); Taylor *et al.* (1992) *J. Mol. Biol.* 226:1287-1290; Takimoto *et al.* (1992), *infra*.

Crystallization conditions suitable to produce diffraction-quality crystals may be selected from a buffer containing, for example: between 1 and 100 mg/ml IL-22 in 10-200 mM buffer (pH 4-9) (*e.g.*, phosphate, cacodylate, acetates, imidazole, Tris HCl, sodium HEPES); and optionally a salt (*e.g.*, calcium chloride, sodium citrate, magnesium chloride, ammonium acetate, ammonium sulfate, potassium phosphate, magnesium acetate, zinc acetate; calcium acetate); and optionally 0-50% of a polymer (*e.g.*, polyethylene glycol (PEG); average molecular weight 200-10,000); and optionally other precipitating agents (salts: potassium or sodium tartrate, ammonium sulfate, sodium acetate, lithium sulfate, sodium formate, sodium citrate, magnesium formate, sodium phosphate, potassium sulfate, ammonium phosphate); and optionally organics *e.g.*, 2-propanol; non-volatile: 2-methyl-2,4-pentanediol).

The above mixtures are used and screened by varying at least one of pH, buffer type; buffer concentration, precipitating salt type or concentration, PEG type, PEG concentration, and protein concentration. Crystals ranging in size from 0.2-0.7 mm are formed in 1-7 days. From one to ten crystals are observed in one drop and crystal forms,

such as, but not limited to, bipyramidal, rhomboid, and cubic, are suitable. Initial X-ray analyses indicate that such crystals diffract at moderately high to high resolution. When fewer crystals are produced in a drop, they can be much larger size, *e.g.*, 0.4-0.9 mm. These crystals diffract X-rays to at least 3.5 Å resolution, such as 1.5-3.5 Å, or any range of value therein, such as 1.5, 1.6, 1.7, 1.8, 1.9, 2.0, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, or 3.0, with 3.0 Å or less being preferred.

## 2. X-ray Diffraction and Structure Determination.

The X-ray diffraction patterns of the invention are of sufficiently high resolution for three-dimensional modeling of IL-22 and IL-22-related molecules, such as IL-22-receptor ligands and IL-22-receptor-chain mimics. Preferably the resolution is in the range of 1.5 to 3.5 Å, more preferably 1.5-3.0 Å and most preferably about 1.9 Å.

X-rays may be produced by high-voltage tubes in which an anode emits X-rays of a specific wavelength upon bombardment by accelerating electrons. More powerful X-ray beams can be produced in synchrotron storage rings where electrons (or positrons) travel near the speed of light. These particles emit very strong radiation at all wavelengths—from short gamma rays to visible light. When used as an X-ray source, however, only X-ray radiation is channeled from the storage ring. Polychromatic X-ray beams are produced by having a broad window that allows through X-ray radiation with wavelengths of 0.2-3.5 Å.

In diffraction experiments, a narrow and parallel beam of X-rays is taken out from the X-ray source and directed onto the crystal to produce diffracted beams. The incident primary beam causes damage to both protein and solvent molecules. The crystal is, therefore, usually cooled to prolong its lifetime (*e.g.*, -220 to -50 °C). The primary beam must strike the crystal from many different directions to produce all possible diffraction spots, and so the crystal is rotated in the beam during the experiment.

The diffracted spots are recorded either on a film, the classical method, or by an electronic detector. The exposed film is measured and digitized by a scanning device, whereas electronic detectors feed the signals they detect directly in a digitized form into

a computer. Electronic area detectors significantly reduce the time required for data collection.

When the primary beam from an X-ray source strikes the crystal, some of the X-rays interact with the electrons on each atom and cause them to oscillate. The oscillating electrons serve as a new source of X-rays, which are emitted in almost all directions, referred to as scattering. When atoms and their electrons are arranged in a regular three-dimensional array, the X-rays emitted from the oscillating electrons interfere with one another. In most cases, these X-rays, colliding from different directions, cancel each other out; those from certain directions, however, will add together to produce diffracted beams of radiation that can be recorded as a pattern on a photographic plate or detector.

The diffraction pattern obtained in an X-ray experiment is related to the crystal that caused the diffraction. X-rays that are reflected from adjacent planes travel different distances, and diffraction only occurs when the difference in distance is equal to the wavelength of the X-ray beam. This distance is dependent on the reflection angle, which is equal to the angle between the primary beam and the planes.

The relationship between the reflection angle ( $\theta$ ), the distance between the planes ( $d$ ), and the wavelength ( $\lambda$ ) is given by Bragg's law:  $2d\sin\theta = \lambda$ . This relationship can be used to determine the size of the unit cell in the crystal. Briefly, the position on the film of the diffraction data relates each spot to a specific set of planes through the crystal. By using Bragg's law, these positions can be used to determine the size of the unit cell.

Each atom in a crystal scatters X-rays in all directions, and only those that positively interfere with one another, according to Bragg's law, give rise to diffracted beams that can be recorded as a distinct diffraction spot above background. Each diffraction spot is the result of interference of all X-rays with the same diffraction angle emerging from all atoms. For the protein crystal of myoglobin, for example, each of the about 20,000 diffracted beams that have been measured contain scattered X-rays from each of the around 1500 atoms in the molecule. To extract information about individual atoms from such a system requires considerable computation. The mathematical tool that is used to handle such problems is called the Fourier transform.

Each diffracted beam, which is recorded as a spot on the film, is defined by three properties: the amplitude, which we can measure from the intensity of the spot; the wavelength, which is set by the X-ray source; and the phase, which is lost in X-ray experiments. All three properties are needed for all of the diffracted beams, in order to determine the position of the atoms giving rise to the diffracted beams.

For larger molecules, protein crystallographers have determined the phases in many cases using a method called multiple isomorphous replacement (MIR) (including heavy metal scattering), which requires the introduction of new X-ray scatterers into the unit cell of the crystal. These additions are usually heavy atoms that contribute significantly to the diffraction pattern. Since such heavy metals contain many more electrons than the carbon, hydrogen, oxygen, nitrogen and sulfur atoms of the protein, they scatter X-rays more strongly. All diffracted beams would therefore increase in intensity after heavy-metal substitution if all interference were positive. In fact, however, some interference is negative; consequently, following heavy-metal substitution, some spots measurably increase in intensity, others decrease, and many show no detectable difference. Isomorphous replacement is usually done by diffusing different heavy-metal complexes into the channels of the preformed protein crystals. The protein molecules expose side chains (such as SH groups) into these solvent channels that are able to bind heavy metals. It is also possible to replace endogenous light metals in metalloproteins with heavier ones, *e.g.*, zinc by mercury, or calcium by samarium.

Phase differences between diffracted spots can be determined from intensity changes following heavy-metal substitution. First, the intensity differences are used to deduce the positions of the heavy atoms in the crystal unit cell. Fourier summations of these intensity differences give maps of the vectors between the heavy atoms—the so-called Patterson maps. From these vector maps the atomic arrangement of the heavy atoms is deduced. From the positions of the heavy metals in the unit cell, one can calculate the amplitudes and phases of their contribution to the diffracted beams of protein crystals containing heavy metals.

This knowledge is then used to find the phase of the contribution from the protein in the absence of the heavy-metal atoms. As both the phase and amplitude of the heavy

metals, the amplitude of the protein alone, and the amplitude of the protein plus heavy metals is known, one phase and three amplitudes are known. From this, the interference of the X-rays scattered by the heavy metals and protein can be calculated to see if it is constructive or destructive. The extent of positive or negative interference, with knowledge of the phase of the heavy metal, gives an estimate of the phase of the protein. Because two different phase angles are determined and are equally good solutions, a second heavy-metal complex can be used which also gives two possible phase angles. Only one of these will have the same value as one of the two previous phase angles; it therefore represents the correct phase angle. In practice, more than two different heavy-metal complexes are usually made in order to give a reasonably good phase determination for all reflections. Notably, each individual phase estimate contains experimental errors arising from errors in the measured amplitudes, and for many reflections, the intensity differences are too small to measure after one particular isomorphous replacement.

The amplitudes and the phases of the diffraction data from the protein crystals are used to calculate an electron-density map of the repeating unit of the crystal. This map then has to be interpreted as a polypeptide chain with a particular amino acid sequence. The interpretation of the electron-density map is complicated by several limitations of the data. First of all, the map itself contains errors, mainly due to errors in the phase angles. In addition, the quality of the map depends on the resolution of the diffraction data, which depends on crystal quality and degree of order. This directly influences the image that can be produced. The resolution is measured in Ångstrom units—as this number decreases, the resolution increases and consequently, the amount of molecular detail observed also increases.

Building the initial model begins by determining how the polypeptide chain weaves its way through the electron-density map. The resulting chain trace constitutes a hypothesis, by which one tries to match the density of the side chains to the known sequence of the polypeptide. When a reasonable chain trace has finally been obtained, an initial model is built to give the best fit of the atoms to the electron density. Computer graphics are used both for chain tracing and for model building to present the data and manipulate the models.

The initial model will contain some errors. Provided the protein crystals diffract to a sufficiently high resolution—better than 3.5 Å—most or substantially all of the errors can be removed by crystallographic refinement of the model using computer algorithms. In this process, the model is modified to minimize the difference between the experimentally observed diffraction amplitudes and those calculated for a hypothetical crystal containing the model, instead of the real molecule. This difference is expressed as an R factor (residual disagreement), which is 0.0 for exact agreement and about 0.59 for total disagreement.

In general, the R factor is preferably between 0.15 and 0.35, and more preferably between about 0.24-0.28 for a well-determined protein structure. The residual difference is a consequence of errors and imperfections in the data. These derive from various sources, including slight variations in the conformation of the protein molecules, as well as inaccurate corrections both for the presence of solvent and for differences in the orientation of the microcrystals from which the crystal is built. This means that the final model represents an average of molecules that are slightly different both in conformation and orientation. In refined structures at high resolution, there are usually no major errors in the orientation of individual residues, and the estimated errors in atomic positions are usually around 0.1-0.2 Å, provided the amino acid sequence is known. Hydrogen bonds, both within the protein and to bound ligands, can be identified with a high degree of confidence.

Most X-ray structures are determined to a resolution between 1.7 Å and 3.5 Å. Electron-density maps with this resolution range are preferably interpreted by fitting the known amino acid sequences into regions of electron density in which individual atoms are not resolved.

The IL-22 crystals are analyzed using a suitable X-ray source and diffraction patterns are obtained. Crystals are preferably stable for at least 10 hrs in the X-ray beam. Frozen crystals (*e.g.*, -220 to -50 C) could also be used for longer X-ray exposures (*e.g.*, 24-72 hrs), the crystals being relatively more stable to the X-rays in the frozen state. To collect the maximum number of useful reflections, multiple frames are optionally collected as the crystal is rotated in the X-ray beam, *e.g.*, for 24-72 hrs. Larger crystals

(>0.2 mm) are preferred, to increase the resolution of the X-ray diffraction. Alternatively, crystals may be analyzed using a synchrotron high-energy X-ray source. Using frozen crystals, X-ray diffraction data is collected on crystals that diffract to a relatively high resolution of 3.5 Å or less, sufficient to solve the three-dimensional structure of IL-22 in considerable detail, as presented herein. Specifically, crystals were soaked in different cryosoaking solutions, mounted in a rayon loop and finally flash-cooled to 80 K in a cold nitrogen stream. Data collection was performed at the Protein Crystallography beamline (LNLS, Campinas, Brazil; Polikarpov *et al.* (1997) *J. Synchrotron Rad.* **5**: 72-76; Polikarpov *et al.* (1997) *Nucl. Instrum. Methods A* **405**: 159-164) and at the X4A beamline (NSLS, Upton, USA), using a MAR345 image plate and a Quantum-4 CCD detector.

The heavy metal derivatives are used to determine the phase, *e.g.*, by the isomorphous replacement method. Heavy atom isomorphous derivatives of IL-22 are used for X-ray crystallography, where the structure is solved using one or several derivatives, which, (when combined) improves the overall figure of merit. Derivatives are identified through Patterson maps and/or cross-phase difference Fourier maps, *e.g.*, using commercially-available software, including the CCP4 package (SERC Collaborative Computing Project No. 4, Daresbury Laboratory, UK, 1979); SIRAS; SHARP [35]; DREAR [31] and SnB 2.1 [32]; and SOLOMON [36]. The program MLPHARE (Wolf *et al.*, eds., Isomorphous Replacement and Anomalous Scattering: Proceedings of CCP4 Study Weekend, pp. 80-86, SERC Daresbury Lab., UK (1991)) is optionally used for refinement of the heavy atom parameters and the phases derived from them by comparing at least one of completeness (%), resolution (in Å),  $R^i$  (%), heavy atom concentration (mM), soaking time, heavy atom sites, phasing power (acentric, centric). Addition of heavy atom derivatives produce an MIR map with recognizable features.

Once the initial phases are calculated to 3.2 Å, they may be improved and extended to a higher resolution of 2.8 Å, using solvent flattening, histogram matching and/or Sayre's equation in the program DM. *See e.g.*, Cowtan *et al.* (1993) *Acta Crystallogr.* **49**: 148-157. The skeletonization of the DM procedure is optionally used to improve connectivity in the bulk of the protein envelope. Both the MIR and density

modified maps are optionally used in subsequent stages, to provide sufficient resolution and/or modeling of surface structures.

Skeletonized representations of electron density maps are then computed. These maps are automatically or manually edited using suitable software, *e.g.*, the graphics package FRODO (Jones *et al.* (1991), *infra*) to give a continuous C $_{\alpha}$  trace. The IL-22 sequence is then aligned to the trace. Initially pieces of idealized polypeptide backbone were placed into regions of the electron density map with obvious secondary structures (*e.g.*,  $\alpha$ -helix,  $\beta$ -sheet). After a polyalanine model was constructed for the protein, amino acid side-chains were added where density was present in the maps. The amino acid sequence of IL-22 was then examined for regions with distinct side-chain patterns (*e.g.*, three consecutive aromatic rings). When a pattern in the sequence was found to match an area of the map, the correct side-chains were built onto the existing model. Eventually fragments containing recognizable sequence motifs were connected into a single chain, completing the tracing of the amino acid sequence into the maps. Cycles of simulated annealing against these data may be refined using the program X-PLOR for molecular dynamics for R-factor refinement. *See e.g.*, Brünger *et al.* (1987) *J. Mol. Biol.* **203**: 803-816. This refinement was followed by manual rebuilding with FRODO using experimental and 2F $_o$  - F $_c$  maps. The model may be further refined using a least-squares refinement program, such as TNT. *See e.g.*, Tronrud *et al.* (1987) *Acta Crystallogr. A* **43**: 489-501. One or more of the above modeling steps may be performed to provide a molecular 3-D model of IL-22. It is preferred that the IL-22 model has no residues in disallowed regions of the Ramachandran plot, and gives a positive 3D-1D profile (Luthy *et al.* (1992) *Nature* **356**: 83-85; Kraulis (1991), *infra*), suggesting that all the residues are in acceptable environments.

Alternatively, a program such as ARP (Lamzin *et al.* (1993) *Acta Cryst.* **D49**: 129-147) may be used to add crystallographic waters and as a tool to check for bad areas in the model. The programs PROCHECK (Lackowski *et al.* (1993) *J. Appl. Cryst.* **26**: 283-291), WHATIF (Vriend (1990) *J. Mol. Graph.* **8**: 52-56), PROFILE 3D (Luthy *et al.* (1992) *Nature* **356**: 83-85), and ERRAT (Colovos *et al.* (1993) *Protein Science* **2**: 1511-1519), as well as the geometrical analysis generated by X-PLOR were used to check the structure for errors. Anisotropic scaling between F $_{obs}$  and F $_{calc}$  may be applied



after careful assessment of the quality and completeness of the data. The program DSSP may be used to assign the secondary structure elements (Kabsch *et al.* (1983) *Biopolymers* **22**: 2577-2637). A program such as SUPPOS (from the BIOMOL crystallographic computing package) can be used for some or all of the least-squares superpositions of various models and parts of models. The program ALIGN (Cohen (1986) *J. Mol. Biol.* **190**: 593-604) may be used to superimpose N- and C-terminal domains of IL-22. Solvent accessible surfaces and electrostatic potentials can be calculated using such programs as GRASP (Nicholls *et al.* (1991), *infra*).

### 3. Rational Drug Design and Molecular Modeling of IL-22 and IL-22-Related

#### Proteins.

Three-dimensional modeling is performed using the diffraction coordinates from the X-ray diffraction patterns and atomic coordinates of the present invention. The coordinates are entered into one or more computer programs for molecular modeling, as known in the art. Such molecular modeling can utilize known X-ray diffraction molecular modeling algorithms or molecular modeling software to generate atomic coordinates corresponding to the three-dimensional structure of at least one IL-22 or a fragment thereof.

The entry of the coordinates of the X-ray diffraction patterns and the amino acid sequence into such programs results in the calculation of the most probable secondary, tertiary and quaternary structures of the protein, including overall atomic coordinates of a IL-22 or a fragment thereof. These structures are combined and refined by additional calculations using such programs to determine the probable or actual three-dimensional structure of the IL-22, including potential or actual active or binding sites of the protein.

Such molecular modeling and related programs useful for rational drug design of ligands or mimetics, are contemplated by the present invention. The drug design uses computer modeling programs which calculate how different molecules interact with the various sites of the IL-22, how IL-22 monomers interact with other IL-22 monomers, how IL-22 interacts with IL-22-receptor mimetics and IL-22 receptors. This procedure determines potential ligands or mimetics of a IL-22. The actual IL-22-ligand complexes

or mimetics are crystallized and analyzed using X-ray diffraction. The diffraction pattern coordinates are similarly used to calculate the three-dimensional interaction of a ligand and the IL-22.

An amino acid sequence of a IL-22 protein and/or X-ray diffraction data, useful for computer molecular modeling of IL-22, can be "provided" in a variety of mediums to facilitate use thereof. As used herein, provided refers to a manufacture, which contains, for example, a IL-22 amino acid sequence and/or atomic coordinate/X-ray diffraction data of the present invention, e.g., an amino acid sequence of SEQ ID NO: 2, a representative fragment thereof, or an amino acid sequence having at least 80-100% overall identity to an amino acid sequence of SEQ ID NO: 2. Such a method provides the amino acid sequence and/or X-ray diffraction data in a form which allows a skilled artisan to analyze and molecular model the three-dimensional structure of a IL-22-related protein, including one or more subdomains thereof.

In one application of this embodiment, IL-22, or at least one subdomain thereof, amino acid sequence and/or X-ray diffraction data of the present invention is recorded on computer readable medium. As used herein, "computer readable medium" refers to any medium which can be read and accessed directly by a computer. Such media include, but are not limited to: magnetic storage media, such as floppy discs, hard disc storage medium, and magnetic tape; optical storage media such as optical discs or CD-ROM; electrical storage media such as RAM and ROM; and hybrids of these categories such as magnetic/optical storage media. A skilled artisan can readily appreciate how any of the presently known computer readable mediums can be used to create a manufacture comprising computer readable medium having recorded thereon an amino acid sequence and/or X-ray diffraction data of the present invention.

As used herein, "recorded" refers to a process for storing information on computer readable medium. A skilled artisan can readily adopt any known method for recording information on computer readable medium to generate manufactures comprising an amino acid sequence and/or atomic coordinate/X-ray diffraction data information of the present invention. A variety of data storage structures are available to a skilled artisan for creating a computer readable medium having recorded thereon an

amino acid sequence and/or atomic coordinate/X-ray diffraction data of the present invention. The choice of the data storage structure will generally be based on the means chosen to access the stored information. In addition, a variety of data processor programs and formats can be used to store the sequence and X-ray data information of the present invention on computer readable medium. The sequence information can be represented in a word processing text file, formatted in commercially-available software such as WordPerfect and MICROSOFT Word, or represented in the form of an ASCII file, stored in a database application, such as DB2, Sybase, Oracle, or the like. A skilled artisan can readily adapt any number of dataprocessor structuring formats (e.g. text file or database) in order to obtain computer readable medium having recorded thereon the information of the present invention.

By providing computer readable medium having stored thereon an IL-22 or related sequence protein and/or atomic coordinates based on X-ray diffraction data, a skilled artisan can routinely access the sequence and atomic coordinate or X-ray diffraction data to model a IL-22 or related protein, a subdomain thereof, mimetic, or a ligand thereof. Computer algorithms are publicly and commercially available which allow a skilled artisan to access this data provided in a computer readable medium and analyze it for molecular modeling and/or RDD. *See, e.g., Biotechnology Software Directory, MaryAnn Liebert Publ., New York (1995).* A variety of comparing means can be used to compare a target sequence or target motif with the data storage means to identify structural motifs or electron density maps derived in part from the atomic coordinate/X-ray diffraction data. A skilled artisan can readily recognize that any one of the publicly available computer modeling programs can be used as the search means for the computer-based systems of the present invention.

Several approaches can be taken for the use of the crystal structure of a IL-22 in the rational design of a relevant activity similar to that of the unmutated IL-22. A computer-assisted, manual examination of an IL-22-receptor-binding site structure is optionally done. Software such as GRID (Goodford (1985) *J. Med. Chem.* **28**: 849-857), a program that determines probable interaction sites between probes with various functional group characteristics and the protein surface, is used to analyze the surface sites to determine structures of similar inhibiting proteins or compounds. The GRID

calculations, with suitable inhibiting groups on molecules (e.g., protonated primary amines) as the probe, are used to identify potential hotspots around accessible positions at suitable energy contour levels.

A therapeutic IL-22 or related protein of the present invention can be, but is not limited to, IL-22-receptor ligands that bind to IL-22 receptors as either agonists or antagonists; IL-22-receptor-chain mimetics or antibodies that bind to endogenous IL-22 and impairs the binding of IL-22 to endogenous receptors. The program DOCK (Kuntz *et al.* (1982) *J. Mol. Biol.* 161: 269-288) may be used to analyze receptor binding sites, dimerization interfaces and/or ligand binding site and suggest ligands or amino acid residues with complementary steric properties. Several methodologies for searching three-dimensional databases to test pharmacophore hypotheses and select compounds for screening are available. These include the program CAVEAT (Bacon *et al.* (1992) *J. Mol. Biol.* 225: 849-858), which uses databases of cyclic compounds which can act as "spacers" to connect any number of chemical fragments already positioned in the active site. This allows one skilled in the art to quickly generate hundreds of possible ways to connect the fragments already known or suspected to be necessary for tight binding. The program LUDI (Bohm *et al.* (1992) *J. Comput.-Aid. Mol. Des.* 6: 61-78) can determine a list of interactions sites into which to place both hydrogen bonding and hydrophobic fragments. LUDI then uses a library of approximately 600 linkers to connect up to four different interaction sites into fragments. Then smaller "bridging" groups such as --CH2-- and --COO-- are used to connect these fragments. For example, for the enzyme DHFR, the placements of key functional groups in the well-known inhibitor methotrexate were reproduced by LUDI. *See also*, Rothstein *et al.* (1992) *J. Med. Chem.* 36: 1700-1710.

Once IL-22-receptor ligands or mimetics are identified, crystallographic studies of, the IL-22 ligand and its receptor complex and the IL-22-receptor mimetic and its IL-22 complex may be performed to confirm and refine the ligand or mimetic properties. Direct measurements of receptor binding or complex formation provide further confirmation that the modeled mimetic and ligands are high affinity IL-22 agonists, antagonists or inhibitors. Any suitable assay for receptor binding or complex formation may be used. The atomic coordinates of IL-22 are useful in the generation of molecular models of related proteins and of IL-22-receptor mimetics and ligands. Utilizing

CLUSTAL (a multiple sequence alignment program in PC-Gene) and the Homology module (a structure-based homology modeling program in InsightII on a Silicon Graphics Incorporated workstation), molecular models (and the corresponding three-dimensional coordinates files) of numerous mimetics and ligands are generated. With these files, mutants and mimetics of the present invention are mapped and new ones designed. The results described herein demonstrate that tight-binding mimetics and ligands of an IL-22 receptor, or related protein, based on the crystal structure of IL-22, are provided by the present invention.

The term "antibody" as used herein, unless indicated otherwise, is used broadly to refer to both antibody molecules and a variety of antibody-derived molecules. Such antibody-derived molecules comprise at least one variable region (either a heavy chain or light chain variable region) and include molecules such as Fab fragments, F(ab)<sub>2</sub> fragments, single chain (sc) antibodies, diabodies, triabodies, tetrabodies, individual antibody light chains, individual antibody heavy chains, chimeric fusions between antibody chains and other molecules, and the like. As used herein "antigen-binding fragment" or "antigen-binding domain" or "Fab fragment" refer to the about 45 kDa fragment obtained by papain digestion of an immunoglobulin molecule and consist of one intact light chain linked by disulfide bond to the n-terminal portion of the contiguous heavy chain. As used herein, "F(ab)<sub>2</sub> fragment" refers to the about 90 kDa protein produced by pepsin hydrolysis of an immunoglobulin molecule. It consists of the N-terminal pepsin cleavage product and contains both antigen binding fragments of a divalent immunoglobulin, such as IgD, IgE, and IgG. Neither the "antigen-binding fragment" nor "F(ab)<sub>2</sub> fragment" contain the about 50 kDa F<sub>c</sub> fragment produced by papain digestion of an immunoglobulin molecule that contains the c-terminal halves of the immunoglobulin heavy chains, which are linked by two disulfide bonds, and contain sites necessary for complement fixation.

As used herein, the term "humanized" antibody refers to a molecule that has its CDRs—complementarily determining regions—derived from a non-human-species immunoglobulin and the remainder of the antibody molecule derived mainly from a human immunoglobulin. As used herein "immunoglobulin" refers to any member of a group of glycoproteins occurring in higher mammals that are major components of the

immune system. As used herein, “immunoglobulins” comprise four polypeptide chains- 2 identical light chains and two identical heavy chains that are linked together by disulfide bonds. An immunoglobulin consists of the antigen binding domains, which are each comprised of the light chains and the end-terminal portion of the heavy chain, and the F<sub>c</sub> region, which is necessary for a variety of functions, such as compliment fixation. There are five classes of immunoglobulins wherein the primary structure of the heavy chain, in the F<sub>c</sub> region, determines the immunoglobulin class. Specifically, the alpha, delta, epsilon, gamma, and mu chains correspond to IgA, IgD, IgE, IgG and IgM, respectively. As used herein “immunoglobulin” includes all subclasses of alpha, delta, epsilon, gamma, and mu and also refers to any natural (*e.g.*, IgA and IgM) or synthetic multimers of the four-chain immunoglobulin structure.

As used herein, “Fv or Fv fragment” refers to the N-terminal part of the Fab fragment of an immunoglobulin molecule, consisting of the variable region of the heavy chain and the variable region of the light chain. As used herein, “scFv” refers to a polypeptide comprising the heavy chain variable region and light chain variable region of a parent immunoglobulin, wherein the heavy chain variable region and the light chain variable region are linked by a peptide linker. As used herein, “diabody” refers to an scFv dimer. As used herein, “triabody” refers to an scFv trimer, and “tetrabody” refers to an scFv tetramer. As used herein, “heavy chain” refers to the heavier of the two types of polypeptide chain in immunoglobulin molecules that contain the antigenic determinants that differentiate the various Ig classes, *e.g.*, IgA, IgD, IgE, IgG, IgM, and the domains necessary for compliment fixation placental transfer, mucosal secretion, and interaction with F<sub>c</sub> receptor. As used herein, “heavy chain variable region” refers to the amino-terminal domain of heavy chain that is involved in antigen binding and combines with the light chain variable region to form the antigen binding domain of the immunoglobulin. As used herein, “light chain” refers to the shorter of the two types of polypeptide chain in an Ig molecule of any class. Light chains comprise variable and constant regions. As used herein, “light chain variable region” refers to the amino-terminal domain of the light chain and is involved in antigen binding and combines with the heavy chain to form the antigen binding region.

The term "variable region" as used herein in reference to immunoglobulin molecules has the ordinary meaning given to the term by the person of ordinary skill in the art of immunology. Both antibody heavy chains and antibody light chains may be divided into a "variable region" and a "constant region." The point of division between a variable region and a constant region may readily be determined by the person of ordinary skill in the art by reference to standard texts describing antibody structure, *e.g.* Kabat *et al.* (1991) Sequences of Proteins of Immunological Interest. 5th Edition. U.S. Department of Health and Human Services, U.S. Government Printing Office.

The recombinant production of immunoglobulin molecules, including humanized antibodies are described in U.S. Pat. No. 4,816,397 (Boss *et al.*), U.S. Pat. No. 4,816,567 (Cabilly *et al.*) U.K. patent GB 2,188,638 (Winter *et al.*), and U.K. patent GB 2,209,757; all of which are incorporated herein by reference. Techniques for the recombinant expression of immunoglobulins, including humanized immunoglobulins, can also be found, among other places in Goeddel *et al.* (1991) Gene Expression Technology, Methods in Enzymology Vol. 185, and Borreback (1992) Antibody Engineering, W. H. Freeman, all of which are incorporated herein by reference. Additional information concerning the generation, design and expression of recombinant antibodies can be found in Mayforth (1993) Designing Antibodies, Academic Press, San Diego and Harlow (1988) Antibodies—A laboratory manual. First Edition. Cold Spring Harbor Laboratory, all of which are incorporated herein by reference.

Without further description, it is believed that one of ordinary skill in the art can, using the preceding description and the following illustrative examples, make and utilize the compounds of the present invention and practice the claimed methods. The following working examples therefore, specifically point out preferred embodiments of the present invention, and are not to be construed as limiting in any way the remainder of the disclosure.

## EXAMPLES

### Example 1: Protein expression and purification.

A cDNA encoding IL-22 sequence lacking the signal peptide was subcloned into the *E. coli* expression vector pET2a, generating pEThtIF. The recombinant protein expressed from this vector contains a methionine at the N-terminus, followed by the amino acid sequence starting at Gln29 to the C-terminus. Vector pEThtIF was transformed into *E. coli* strain BL21 (DE3)-codon plus-RIL. The resulting strain was maintained in LB medium containing Ampicillin (100 µg/ml) and Chloramphenicol (34 µg/ml). Induction of IL-22 express was performed at 37°C for 4 hours with 1 mM IPTG, which was added when the cultures reached an OD<sub>660</sub> of approximately 1.0-1.3. Under these conditions, up to 50 mg/l of IL-22 were obtained. Cells were lysed by using a high pressure cell (French Press) and the inclusion bodies were washed once in buffer containing 50 mM Tris-HCl, pH 8.0, 100 mM NaCl, 1 mM EDTA, 1 mM DTT and 0.5% sodium deoxycholate and once in the same buffer lacking sodium deoxycholate. The inclusion bodies were solubilized in 25 mM MES pH 5.5, 8 M urea, 10 mM EDTA, and 0.1 mM DTT. Protein concentration was adjusted to 100 µg/ml and refolded by dialysis in buffer containing Tris-HCl pH 8.0, 0.5 M arginine, 1 mM reduced glutathione, 0.1 mM oxidized glutathione, 2 mM EDTA and 0.1 mM PMSF. Refolding was performed for 20 h at 4°C. Refolded samples were concentrated 100 fold with a YM3 AMICON membrane and loaded onto a Superdex 75 10/30 HP column (Amersham-Pharmacia), which was eluted with buffer containing 25 mM MES pH 5.4 and 150 mM NaCl. Human IL-22 peak fractions were concentrated to 5 mg/ml with a YM3 AMICON membrane and desalted using a Hiprep 26/10 column (Amersham-Pharmacia) with elution buffer containing 10 mM MES pH 5.4. Human IL-22 was concentrated again to 5 mg/ml and lyophilized in 1 mg fractions.

### Example 2: Protein crystallization.

Preliminary screening of the crystallization conditions was performed using a sparse-matrix screen at 291 K (Crystal Screen I and II, Hampton Research Corp.). Small



crystals were found in the condition number 18, 26 and 29 of the Crystal Screen I kit. Several attempts to enhance crystal quality were performed, including pH and precipitant concentration refinement, detergent addition, and macroseeding. Well diffracting crystals were obtained in hanging drops equilibrated against a reservoir solution consisting of 0.9 M sodium tartrate, TRITON X-100 detergent and 0.1 M HEPES at pH 7.5. The crystallization drops contained equal volumes (1 $\mu$ l) of reservoir and purified IL-22 (10 mg/ml in 20 mM MES buffer at pH 5.4) solutions. The protein crystallized in the space group P2<sub>1</sub>2<sub>1</sub>2<sub>1</sub>, with unit-cell dimensions a=55.43, b=61.61, c=73.43 Å.

### Example 3: Data collection.

Crystals were soaked in different cryosoaking solutions, mounted in a rayon loop and finally flash-cooled to 80°K in a cold-nitrogen stream. Data collection was performed at the Protein Crystallography beamline (LNLS, Campinas, Brazil; Dumoutier *et al.* (2000) *Genes and Immunity* 1: 488-494; Cookson, (2000) *Nature* 402s: B5-B11) and at the X4A beamline (NSLS, Upton, USA), using a MAR345 image plate and a Quantum-4 CCD detector, respectively. Three diffraction datasets were collected to a resolution beyond 1.95 Å. Diffraction images were processed and scaled with the programs DENZO and SCALEPACK. *See e.g.*, Walter *et al.* (1995) *Biochemistry* 34: 12118-12125.

### Example 4: Heavy-atom derivatives and phasing.

The structure was solved by SIRAS. An iodine derivative was obtained by soaking the crystal for 180 seconds in 2 $\mu$ l of cryoprotectant solution containing 0.125 M sodium iodide following the novel “quick cryo soaking” derivatization procedure. *See e.g.*, Kotenko *et al.* (1997) *EMBO J.* 16: 5894-5903; Zdanov *et al.* (1995) *Structure* 3: 591-601. The data sets of an iodine derivative (I-IL-22) and a native crystal (Nat-IL-22) were collected at the Protein Crystallography beamline (Dumoutier *et al.* (2000) *Genes and Immunity* 1: 488-494; Cookson (2000) *Nature* 402s: B5-B11) at LNLS (Campinas, São Paulo, Brazil). The heavy-atom positions of the iodine derivative were determined by direct methods with the programs DREAR (Ealick *et al.* (1991) *Science* 252: 698-

702) and SnB 2.1 (Josephson *et al.* (2000) *J. Biol. Chem.* **275**: 13552-13557). The bimodal distribution of the  $R_{\min}$  histogram was used to identify the correct solution (Tr  ze (1999) The cytokine network and immune functions. Oxford University Press, Oxford; Barton, (1993) *Protein Eng.* **6**: 37-40). The heavy-atom substructure obtained directly from SnB was initially refined with the CNS package using anomalous and isomorphous difference Fourier maps. Refined coordinates were then input into SHARP (Otwinowski *et al.* (1997) *Methods Enzymol.* **276**: 307-326) for phase calculation, resulting in an overall figure of merit of 0.45 for all reflections in the range of 21.7 – 2.40  . Density modification with solvent flattening was performed using the program SOLOMON. *See e.g.*, Blessing, *et al.* (1999) *J. Appl. Cryst.* **32**: 664-670. Due to the high resolution and completeness of the I-IL-22 data set, and also the quality of solvent-flattened electron-density map, an automatic construction of an IL-22-hybrid model could be performed by the ARP/wARP program. *See e.g.*, Thiel, *et al.* (2000) *Structure* **8**: 927-936. The nucleotide-based IL-22 primary structure was used in the final-model-side-chain assignment. *See e.g.*, Dumoutier *et al.* (2000) *Proc. Natl. Acad. Sci. U.S.A.* **97**: 10144-10149.

One mercury derivative was also obtained using traditional methods of derivatization. The Hg derivative (Hg-IL-22) data set was collected at the X4A beamline at NSLS (Upton, New York, USA) and was used at latter stages of refinement and construction of disordered loops. This latter derivative was prepared using traditional methods for derivatization of protein crystals. Details of native and derivative crystal preparation, as well as data statistics, are summarized in Table 1.

### Example 5: Model building.

#### 1. Refinement.

A. The initial model was obtained without manual intervention after 6 ARP/wARP jobs and more than 4000 REFMAC cycles. *See e.g.*, Weeks, *et al.* (1999) *J. Appl. Cryst.* **32**: 120-124. In the last cycle, after almost 72 hours of uninterrupted CPU time in a Pentium III 500 MHz, 81.6% of the total amino acid residues were corrected traced.

**B.** The initial structure of IL-22 was improved by a number of cycles of refinement and rebuilding using CNS package. *See e.g., Polikarpov, et al. (1997) J. Synchrotron Rad.* **5**: 72-76. Interlaced refinement of model against Nat-IL-22, Hg-IL-22 and I-IL-22 data sets were used to allow a complete trace of main chain atoms through disordered regions. The initial model contained 231 amino acid residues (in nine distinct chains) and 809 water molecules. The isolated cDNA of IL-22 encodes a protein of 179 amino acids, of which the first 22 amino acids are predicted to function as a signal sequence. (Xie *et al.* (2000) *J. Biol. Chem.* **275**: 31335-31339). The N-terminal amino acid analysis of IL-22 confirms that the mature protein begins at amino acid residue 34. Construction of disordered loops and filling of main chain gaps were performed manually using the program O. *See e.g., Debaerdemaeker, et al. (1983) Acta Cryst.* **A39**: 193-196. Finally, the model was refined against a Nat-IL-22 data set, starting with a simulated annealing protocol in the program CNS. After several iterations of energy minimization, B-factor refinement, and bulk-solvent and anisotropic corrections, the final  $R_{\text{factor}}$  and  $R_{\text{free}}$  were 0.191 and 0.225, respectively, for the Nat-IL-22 data in the resolution range of 21.7 – 1.92 Å. The final model includes 283 residues (two chains) and 189 water molecules. The refined model of IL-22, a dimer in the asymmetric unit (Fig. 1a), includes monomer A with 142 amino acid residues (Ser38-Ile179), monomer B with 141 amino acid residues (His39-Ile179) and 189 water molecules. About 93.8% and 6.2% of the amino acid residues adopt a conformation that corresponds to the most favored and additionally allowed regions of the Ramachandran plot, respectively. *See e.g., Table 2* for further information about refinement and geometry statistics. No residues have been encountered in the disallowed regions of the Ramachandran plot.

As shown in Figure 1b, each monomer of IL-22 model is characterized by six  $\alpha$ -helices (A-F) that fold in a compact bundle. Helix A (amino acid residues Lys44-Ser64) is linked to a short helix B (Glu77-Pe80) by a large loop AB (Leu65-Gly76). Helix A has a kink at Gln48-Gln49, presumably due to a hydrogen bond between N $\epsilon$ -Gln49 and O-Ser45 (2.79 Å and 2.55 Å in monomers A and B, respectively). This divides helix A into unequal parts: A<sub>1</sub> and A<sub>2</sub>. The loop BC (His81-Glu87) connects helix B to helix C (Arg88-Glu102). The helix C is joined to helix F by a disulfide bond between Cys89 and Cys178. Another loop (CD; Val103-Try114) links helix C to helix D (Met115-Leu129).

According to PROCHECK (Laskowski *et al.* (1993) *J. Appl. Crystallogr.* **26**: 283-291), a small difference in secondary structure between monomers is observed at the loop CD region. A small  $\alpha$ -helix is observed between amino acid residues Phe105 and Gln107 of the monomer B. Helix D is connected to helix E by a disordered loop (DE; Ser130-Asp138). This loop is stabilized, at least in the vicinity of Cys132, by another disulfide bond between Cys132 and Cys40, the latter in the N-terminal coil. Finally, a simple junction EF (Gly156) joins the last two helices E (Leu139-Leu155) and F (Glu157-Cys178). Probably, as a consequence of a disulfide bond between Cys89 and Cys178, the latter belonging to the C-terminal of helix F, a kink at Glu166 divides helix F into two parts: F<sub>1</sub> and F<sub>2</sub>.

## 2. Dimer formation.

An expressive part (61%) of the volume of the asymmetric unit ( $6.27 \times 10^4 \text{ \AA}^3$ ) is occupied by a dimer of IL-22. A small fraction of this volume (8%) is filled with ordered water molecules. The monomers are essentially equal, however, a number of significant differences in the main chain conformation are observed in the vicinity of amino acid residues Gln48, Asn69, Gln136 and Lys154 (Fig. 2). These differences are mostly explained by crystallographic and non-crystallographic contacts. The reason for a significant positional difference between monomers around Gln48 is the fact that this region in monomer A is involved in interface interactions, whereas the same region in monomer B is exposed to the solvent. In addition, the presence of two intramolecular interactions—O $\delta$ 1-Asp43/O $\gamma$ -Ser45 with 2.64  $\text{\AA}$  in monomer A and O-Asn46/N $\epsilon$ 2-Gln49 with 2.55  $\text{\AA}$  in monomer B—contribute to a relative change in main-chain atoms positions between residues Leu42 and Pro50. A second conformational difference around Asn69 is a consequence of a crystallographic contact between side chain atoms of Asn69 and Thr70 of monomers A and B, respectively. Gly136 is localized in the disordered loop DE. This fact explains the root-mean-square-deviation (rmsd) around 2.0  $\text{\AA}$  in the vicinity of this amino acid residue. Finally, the last major difference between monomers is found close to Lys154. In this region, three distinct interactions of Lys153 and Lys154 from monomer B—O $\epsilon$ 1-Glu102/N $\zeta$ -Lys153 with 2.68  $\text{\AA}$ , O $\delta$ 1-Asn46/N $\zeta$ -Lys153 with 2.78  $\text{\AA}$  and O $\epsilon$ 1-Glu160/N $\zeta$ -Lys154 with 2.80  $\text{\AA}$ , which are absent in monomer A—are responsible for a high rmsd of main-chain atoms.

Unlike the hIL-10, the IL-22 dimeric structure formation does not require the intertwining of the main chain of each monomer (Fig. 1). An interface area of approximately 2250 Å<sup>2</sup>, which corresponds to 30% of the total surface area of a monomer, is involved in the dimer formation. The buried surface for the chosen dimer conformation is at least two times larger than any other buried surface area (~ 960 Å<sup>2</sup> or less). Also, the dimer interface, which is formed mostly by residues Arg41 to Phe80 and Asp168 to Ile179 in monomer A and Thr53 to Arg88 and Glu166 to Ile179 in monomer B, has a significant number of hydrophobic residues. Intermolecular interface contacts closer than 3.2 Å are listed in Table 3. The electrostatic and hydrophobic distribution of the IL-22 surface together with the position of the principal amino acid residues involved in the formation of the dimer are given in Fig. 3.

According to the predicted primary structure, human IL-22 has three potential glycosylation sites (Asn-Xaa-Thr/Ser) localized in helix A (Asn54-Arg55-Thr56) (site #1), loop AB (Asn68-Asn69-Thr70) (site #2) and helix C (Asn97-Phe98-Thr99) (site #3). Since the recombinant IL-22 used in crystallization is not glycosylated, we attempted the analysis of the possible interactions between oligosaccharides and IL-22 by calculating the accessible area of each residue in all three putative glycosylation sites. The results demonstrate that site #2, localized at the loop AB, is the one with the larger accessible area. A solvent-accessible area of approximately 37 Å<sup>2</sup> was found for Nδ2-Asn68 and for Oγ1-Thr70 atoms, indicating that there is no steric hindrance to their participation in N-glycosyl and O-glycosyl links, respectively. On the other hand, sites #1 and #3 seem to participate only in N-glycosyl linkages. The accessible area of Oγ1-Thr56 and Oγ1-Thr99 is 0 and 6 Å<sup>2</sup>, whereas Nδ2-Asn54 and Nδ2-Asn97 atoms possess, respectively, the surface-accessible area of 24 and 18 Å<sup>2</sup>. This structural analysis is in agreement with biochemical studies suggesting that these three sites are of N-glycosyl type. (Kotenko *et al.* (2001) *J. Biol. Chem.* **276**: 2725-2732). Consistent with biophysical observations, the present structure shows that putative glycosylation sites #1 and #2 reside near the dimer interface, and that glycosylation at these positions would disrupt dimer formation.

### 3. Comparison of IL-22 to the structures of IL-10 and IFN- $\gamma$ .

As shown in Figure 2, the crystallographic structure of hIL-22 is a compact dimer, with a buried surface area of approximately 2250 Å<sup>2</sup>. Several intermolecular interactions along the interface surface keep the monomers together. Each monomer is formed by six  $\alpha$ -helices (A-F) from the same polypeptide chain. Quite in contrast, the crystallographic structures of hIL-10 (Levitt *et al.* (1999) *J. Allergy Clin. Immunol.* **103**: S485-S491; Laskowski *et al.* (1993) *J. Appl. Crystallogr.* **26**: 283-291; Kraulis *et al.* (1991) *J. appl. Cryst.* **24**: 946-950) and hIFN- $\gamma$  (Esnouf (1997) *J. Mol. Graph.* **15**: 133-138; McLane *et al.* (1998) *Am. J. respir. Cell Mol. Biol.* **19**: 713-720) revealed the presence of a homodimer composed of two  $\alpha$ -helical domains formed by intertwining of  $\alpha$ -helices donated by the first and the second monomer composing a dimer. The first four helices of one chain (A-D), together with the helices E' and F' from the second chain, compose the first domain. Helices A' to D', E and F form the second domain.

There are significant structural similarities between IL-22, IL-10 and IFN- $\gamma$  (Fig. 4). In all these proteins, helices A to D of each monomer form a rigid frame with a highly hydrophobic depression in its middle. This depression is covered in IL-22 by helices E and F from the same monomer, whereas in hIL-10 and hIFN- $\gamma$  this is accomplished by helices E' and F' (from the second monomer). The basic reason for these differences is in the loop DE. There are two cysteine residues Cys126 and Cys132 at the hIL-10 DE loop that make two distinct disulfide bonds with residues Cys30 and Cys80, respectively. (Here we adopted the residue numbering according to the hIL-10 cDNA sequence). These two S-S bridges restrict the flexibility of the amino acid chain and the length of the loop DE in such a manner that helices E and F can not fold onto their respective monomer to occupy position of their counterparts E' and F'. This leads to the intertwined dimer formation. See e.g., Levitt *et al.* (1999) *J. Allergy Clin. Immunol.* **103**: S485-S491; Laskowski *et al.* (1993) *J. Appl. Crystallogr.* **26**: 283-291; Kraulis *et al.* (1991) *J. appl. Cryst.* **24**: 946-950. A monomeric form of hIL-10 could only possibly be created when the Cys80-Cys132 disulfide bond were to be reduced, or if a small amino acid chain were inserted after Cys132. See e.g., Levitt *et al.* (1999) *J. Allergy Clin. Immunol.* **103**: S485-S491. The latter approach has been applied with success to hIL-10, where insertion of a small polypeptide linker in the loop that connects

the swapped secondary structure elements led to the formation of a monomeric protein. See e.g., Merritt, *et al.* (1997) *Methods Enzymol.* **277**: 505-524. Similarly, the hIFN- $\gamma$  intertwined dimer is formed because the loop DE is not long enough to allow the fold of helix E and F into the same domain.

In IL-22, just one disulfide bond (Cys40-Cys132) exists at the loop DE, which allows sufficient flexibility and extension of the loop to bring helices E and F into close contact with helices A to D and to complete the folding of the monomer. A second disulfide bond, in the C-terminal of helix F (Cys89-Cys178), adds to a rigidity of a final IL-22 structure.

The best superposition of IL-22 onto hIL-10 and hIFN- $\gamma$  was obtained using a single domain of the hIL-10 and hIFN- $\gamma$  onto IL-22 yielding an rmsd of 1.9 Å and 2.3 Å for 432 and 300 pairs of main chain atoms, respectively. Helices A to D of the IL-22 monomer superimpose with helices A to D of one of the monomers of hIL-10 and hIFN- $\gamma$ . Helices E and F fit nicely into the spatial position occupied by helices E' and F' of the second monomer. The three-dimensional superposition of the structures allowed us to perform a structure-based sequence alignment for IL-22 and IL-10 that is shown in Figure 5. Inspection of the superposition of IL-22 and hIL-10 revealed strong similarities in the conformation of the main-chain trace of helices E (E') and F (F'), and to a lesser extent, the conformation of several parts of loop AB, helix C and helix D. Each of these regions represent high sequence similarity. Some significant differences in the regions of the N-terminal coil, helix A, helix B, loop BC, loop CD and loop DE were also observed.

Reasonable superposition of hIL-10 or hIFN- $\gamma$  dimers onto IL-22 dimer was proven to be impossible. In each case, dimer formation is so much different that only one domain of IL-22 could be superimposed with an hIL-10 (or hIFN- $\gamma$ ) domain. A second domain of each structure occupies completely different spatial positions (Figs. 4c and 4d). Whereas the intertwining of  $\alpha$ -helices is essential for the formation and integrity of molecules adapting a form of the V-shaped dimers (*i.e.*, hIL-10 and hIFN- $\gamma$ ), in IL-22 dimer formation is not required for folding. It must be stressed that the buried

surface on the hIL-2 interface coincides with the outer part of the hIL-10 and hIFN- $\gamma$  V-shaped-dimer surfaces (Figs. 4c and 4d).

#### 4. Receptor binding sites.

Two receptor chains—CRF2-4 and CRF2-9—have been identified for IL-22. The CRD2-4 receptor chain is common between IL-22 and IL-10 and is necessary for signaling, whereas CRD2-9 is specific for IL-22. *See e.g., Xie et al. (2000) J. Biol. Chem. 275: 31335-31339; Kotenko et al. (2001) J. Biol. Chem. 276: 2725-2732; both incorporated herein by reference.* CRF2-9 bears primary sequence homology to the another receptor chain of IL-10—IL-10R1. The binding affinity of IL-22 and IL-10 to CRF2-4 is different. CRF2-4 alone is sufficient to bind IL-22, while the presence of a second receptor chain is required for efficient IL-10 binding. Moreover, both CRF2-9 and CRF2-4 share significant sequence homology to the IFN- $\gamma$  receptor, IFN- $\gamma$ R $\alpha$ . The three-dimensional structure of hIFN- $\gamma$ R $\alpha$  was recently solved as a complex with its ligand (McLane *et al.* (1998) *Am. J. Respir. Cell Mol. Biol.* 19: 713-720; incorporated herein by reference), and the structure of IL-22 was superimposed onto the structure of the hIFN- $\gamma$ /hIFNR $\alpha$  complex to identify the residues involved in IL-22/receptor interactions. A similar structural comparison with the hGH/hGHBP complex has been used in receptor-binding-site analysis of IL-10. *See e.g., Levitt, et al. (1999) J. Allergy Clin. Immunol.* 103: S485-S491; incorporated herein by reference.

The superposition of IL-22 onto the hIFN- $\gamma$ /hIFNR $\alpha$  complex indicates that one possible receptor binding site is localized in the region formed by helix A, loop AB and helix F of IL-22 (Region 1, R1; see Figures 4d and 6a). Among the 17 residues involved in hIFN- $\gamma$ /hIFNR $\alpha$  interactions (closer than 3.4 Å), only two residues do not have their IL-22 structural counterparts localized in R1. Nine of the seventeen residues localized in R1 are not sufficiently close to their hIFN- $\gamma$  counterparts, which may explain the inability of IL-22 to bind to hIFN- $\gamma$ R $\alpha$ . The major differences between hIFN- $\gamma$  and IL-22 within R1 are observed in the loop AB and distances of more than 7 Å are found between their main chains. As shown in Figure 6b, six relatively conserved residues (Lys61, Thr70, Asp71, Lys162, Glu166 and Leu169), however, occupy almost the same spatial position as six hIFN- $\gamma$  residues—Lys35, Asp47, Asn48, Lys131, Glu135, Gln138.



A comparison with the hIL-10 putative receptor binding site (Levitt, *et al.* (1999) *J. Allergy Clin. Immunol.* **103**: S485-S491; incorporated herein by reference) shows that Region 1—helix A, loop AB and helix F' in the case of hIL-10—is involved in receptor interactions. Amino acid residues Gln60, Asp62, Asn63, Lys156, Glu160, Asp162, Asp166 and Glu169 of the hIL-10 binding site having their IL-22 counterparts in residues Asn68, Thr70, Asp71, Lys162, Glu166, Asp168, Met172 and Arg175. Among these eight residues, Thr70, Asp71, Lys162 and Glu166 were also found in the IL-22:IFN- $\gamma$ /INF- $\gamma$ R $\alpha$  comparison. The superposition of the hIL-10 putative binding Region 1 onto IL-22 is shown in Figure 6c. The three-dimensional structure comparison of IL-22 with either IFN- $\gamma$ /INF- $\gamma$ R $\alpha$  or hGH/hGHBP complexes demonstrates that Region 1 is the receptor binding site.

The three-dimensional similarities observed between IL-22 and hIL-10 in Region 1, especially between helices F and F', also indicate that this region is the CRF2-4 binding site. In addition, the glycosylation site in the IL-22 AB loop may interfere with receptor binding. The homology of INF- $\gamma$ R $\alpha$  CRF2-9 also suggests that R1 is the recognition/binding site for CRF2-9. Notably, in the present crystallographic model, the region 1 of each monomer is hidden at the dimer interface. Moreover, a few potential receptor-binding residues are directly involved in dimer formation (see Table 3). Therefore, a IL-22-receptor chain can only bind a monomer of IL-22, and thus, requires the dissociation of the dimer observed in the present crystallographic structure. In contrast, the hIL-10 dimer does not require disruption prior to interaction with the receptor, since the hIL-10-receptor-binding site is localized at the outer part of the B-shaped-dimer surface (Figures 4c and 4d).

Although the RZ binding site in IL-22 cannot be easily inferred from inspection of the interactions between hINF- $\gamma$  and hINF- $\gamma$ R $\alpha$ , region Z, which comprises the terminal portions of helices C and E of each IL-22 monomer, is a binding site for CRF2-4. A sequence comparison between IL-22 and several IL-10 identifies several amino acids that are conserved within the Region 2 (R2) region—FTLEEV (SEQ ID NO: 4) and KLGE (SEQ ID NO: 5) in IL-22 helices C and E, respectively. Region 2 is localized at the surface of IL-22, which is opposite to R1. Localization of each binding region (R1 and R2) on the opposite sides of the IL-22 molecule allows IL-22 to interact

with two receptor chains simultaneously. In hIL-10, the amino acids corresponding to the region R2 are localized at the inner part of the V-shaped dimer surface. The angle between each hIL-10 domain in the V-shaped dimer is large enough to allow interaction of two CRF2-4 receptor chains with the two binding sites in RZ 2 (Figure 4c).

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**Table 1. Details of the preparation and data-collection statistics of IL-22 crystals. Statistical values for the highest resolution shells are shown in parentheses.**

	<b>Nat-IL-22</b>	<b>I-IL-22</b>	<b>Hg-IL-22</b>
Space group	P2 <sub>1</sub> 2 <sub>1</sub> 2 <sub>1</sub>	P2 <sub>1</sub> 2 <sub>1</sub> 2 <sub>1</sub>	P2 <sub>1</sub> 2 <sub>1</sub> 2 <sub>1</sub>
Unit cell parameters (Å)	a=55.43; b=61.61; a=56.04; b=61.71; c=73.47	a=56.05; b=61.78; c=73.63	c=74.61
Resolution (Å)	21.7 - 1.92 (1.96 - 1.92)	21.8 - 1.92 (1.96 - 1.92)	22.4 - 1.90 (1.97 - 1.90)
No. of reflections	67677	182876	55855
No. of unique reflections <sup>1</sup>	18139	37777	29854
<I/σ(I)>	14.4 (2.5)	13.4 (3.1)	8.2 (2.1)
Multiplicity	3.7 (3.1)	4.8 (4.3)	1.9 (1.7)
Completeness	91.2 (75.1)	99.9 (99.7)	75.9 (77.9)
R <sub>merge</sub> <sup>2</sup>	8.6 (50.8)	11.7 (43.9)	10.0 (49.9)
Data collected (degrees)	103.2	248.6	70.0
Cryoprotectant solution	Mother liquor 15% ethyl. glycol	Mother liquor 15% ethyl. glycol	Mother liquor 15% ethyl. glycol
Soaking time	30 seconds	0.125 M NaI 180 seconds	5 mM HgCl <sub>2</sub> 10 hours

<sup>1</sup> Multiplicity of derivative (native) data sets calculated with Friedel-related reflections treated separately (as equivalent).

$$^2 R_{\text{merge}} = \sum hkl |I_{hkl} - \langle I_{hkl} \rangle| / \sum hkl I_{hkl}$$

Table 2. Refinement statistics and quality of the IL-22 model.<sup>1</sup>**GENERAL INFORMATION**

Disulfide bonds	Cys40-Cys132 and Cys89-Cys178
Cis-peptides	Pro113
Alternative conformations	Met172 in monomer A Asp43, Ser45, Arg55, Ile75, His81, Arg124, Ile161 and Leu174 in monomer B

**REFINEMENT STATISTICS (21.7 – 1.92 Å)**

Total number of reflections	17238
Working set number of reflections	16372
R-factor (%)	19.1
Test set number of reflections	866
R-free (%)	22.5
Total number of protein atoms	2330
Total number of water molecules	189

**GEOMETRY STATISTICS**

Rmsd bond distances (Å)	0.006
Rmsd bond angles (°)	1.1
Average B factors	
residue atoms (Å <sup>2</sup> ) (A, B)	24.3 (22.3, 26.2)
mainchain atoms (Å <sup>2</sup> ) (A, B)	22.1 (20.2, 24.1)
sidechain atoms (Å <sup>2</sup> ) (A, B)	26.3 (24.4, 28.1)
water molecules (Å <sup>2</sup> )	37.3
Average rmsd B factor	
residue atoms (Å <sup>2</sup> ) (A, B)	2.5 (2.6, 2.5)
mainchain atoms (Å <sup>2</sup> ) (A, B)	1.0 (1.0, 1.0)
sidechain atoms (Å <sup>2</sup> ) (A, B)	1.9 (2.0, 1.8)
water molecules (Å <sup>2</sup> )	11.4
Ramachandran plot <sup>2</sup>	
residues in most favored region (%)	93.8
residues in additionally allowed regions (%)	6.2
residues in generously allowed regions (%)	0.0
residues in disallowed regions (%)	0.0

Table 2. Continued<sup>1</sup>

NON-CRYSTALLOGRAPHIC SYMMETRY <sup>3</sup>

Rmsd coordinates	
Cα atoms (Å)	0.911
mainchain atoms (Å)	0.884
all bonded atoms (Å)	1.670
Rmsd B factors	
Cα atoms (Å <sup>2</sup> )	10.04
mainchain atoms (Å <sup>2</sup> )	10.05
all bonded atoms (Å)	10.77

<sup>1</sup> Amino acid residues correspond to residues in human IL-22, SEQ ID NO: 2.

<sup>2</sup> Residue regions as defined by PROCHECK (Laskowski *et al.* (1993) *J. Appl. Crystallogr.* **26**: 283-291).

<sup>3</sup> Non-crystallographic symmetry of subunits A and B.

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Table 3. Intermolecular contacts (monomers A<sup>\*</sup> and B<sup>\*\*</sup>). The distance cut-off of 3.2 Å was used.<sup>1</sup>

Residue <sup>*</sup>	Atom <sup>*</sup>	Residue <sup>**</sup>	Atom <sup>**</sup>	Distance (Å)
Arg175	Nη2	Glu166	Oε1	2.57
Phe57	O	Asn176	Nδ2	2.64
Arg73	Nη2	Val83	O	2.71
Lys44	Nζ	Ser64	Oγ	2.85
Arg175	Nη1	Asp168	Oδ2	2.86
Asn176	Nδ2	Ile75	O	2.91
Gln48	O	Lys61	Cε	2.96
Lys44	Nζ	Glu166	Oε1	2.98
Lys61	Nζ	Ile179	OT1	3.12
Gln49	Oε1	Lys61	Nζ	3.15

<sup>1</sup> Amino acid residues correspond to residues in human IL-22, SEQ ID NO: 2.

<sup>1</sup> Amino acid residues correspond to residues in human IL-22, SEQ ID NO: 2.

Table 4. Atomic Coordinates of human IL-22 determined as described herein.<sup>1</sup>

CRYST1	55.430	61.610	73.470	90.00	90.00	90.00	P 21 21 21
SCALE1	0.01804	0.00000	0.00000			0.00000	
SCALE2	0.00000	0.01623	0.00000			0.00000	
SCALE3	0.00000	0.00000	0.01361			0.00000	
ATOM	1	CB	SER A	38	8.633	14.375	24.449 1.00 47.79
A C							
ATOM	2	OG	SER A	38	8.362	14.381	23.062 1.00 49.55
A O							
ATOM	3	C	SER A	38	8.165	16.820	24.641 1.00 44.87
A C							
ATOM	4	O	SER A	38	7.431	17.426	23.855 1.00 44.76
A O							
ATOM	5	N	SER A	38	6.339	15.165	24.930 1.00 47.40
A N							
ATOM	6	CA	SER A	38	7.787	15.434	25.155 1.00 46.37
A C							
ATOM	7	N	HIS A	39	9.311	17.315	25.099 1.00 42.59
A N							
ATOM	8	CA	HIS A	39	9.807	18.631	24.708 1.00 40.15
A C							
ATOM	9	CB	HIS A	39	10.759	19.164	25.780 1.00 43.57
A C							
ATOM	10	CG	HIS A	39	11.980	18.320	25.978 1.00 46.37
A C							
ATOM	11	CD2	HIS A	39	13.290	18.653	26.075 1.00 48.11
A C							
ATOM	12	ND1	HIS A	39	11.923	16.950	26.124 1.00 48.60
A N							
ATOM	13	CE1	HIS A	39	13.143	16.476	26.302 1.00 49.04
A C							
ATOM	14	NE2	HIS A	39	13.992	17.489	26.276 1.00 48.92
A N							
ATOM	15	C	HIS A	39	10.535	18.557	23.371 1.00 36.84
A C							
ATOM	16	O	HIS A	39	11.370	17.680	23.157 1.00 36.46
A O							
ATOM	17	N	CYS A	40	10.221	19.475	22.465 1.00 32.36
A N							
ATOM	18	CA	CYS A	40	10.875	19.461	21.169 1.00 29.17
A C							
ATOM	19	C	CYS A	40	12.286	20.011	21.292 1.00 26.49
A C							
ATOM	20	O	CYS A	40	12.490	21.114	21.793 1.00 24.81
A O							
ATOM	21	CB	CYS A	40	10.095	20.298	20.162 1.00 29.95
A C							
ATOM	22	SG	CYS A	40	8.366	19.818	19.887 1.00 28.05
A S							
ATOM	23	N	ARG A	41	13.259	19.238	20.828 1.00 24.42
A N							
ATOM	24	CA	ARG A	41	14.648	19.657	20.890 1.00 24.30
A C							
ATOM	25	CB	ARG A	41	15.144	19.580	22.339 1.00 28.36
A C							

ATOM	26	CG	ARG	A	41	16.568	20.046	22.548	1.00	35.78
A	C									
ATOM	27	CD	ARG	A	41	16.733	20.673	23.927	1.00	40.37
A	C									
ATOM	28	NE	ARG	A	41	15.954	21.902	24.052	1.00	43.92
A	N									
ATOM	29	CZ	ARG	A	41	15.888	22.643	25.155	1.00	47.14
A	C									
ATOM	30	NH1	ARG	A	41	16.558	22.282	26.244	1.00	46.80
A	N									
ATOM	31	NH2	ARG	A	41	15.147	23.745	25.169	1.00	49.17
A	N									
ATOM	32	C	ARG	A	41	15.489	18.762	19.990	1.00	22.91
A	C									
ATOM	33	O	ARG	A	41	15.087	17.650	19.668	1.00	22.24
A	O									
ATOM	34	N	LEU	A	42	16.650	19.265	19.578	1.00	20.60
A	N									
ATOM	35	CA	LEU	A	42	17.568	18.528	18.715	1.00	17.57
A	C									
ATOM	36	CB	LEU	A	42	17.411	18.989	17.264	1.00	17.84
A	C									
ATOM	37	CG	LEU	A	42	16.086	18.717	16.557	1.00	18.08
A	C									
ATOM	38	CD1	LEU	A	42	16.074	19.406	15.195	1.00	17.09
A	C									
ATOM	39	CD2	LEU	A	42	15.902	17.218	16.405	1.00	18.48
A	C									
ATOM	40	C	LEU	A	42	18.992	18.814	19.184	1.00	16.85
A	C									
ATOM	41	O	LEU	A	42	19.391	19.973	19.306	1.00	18.05
A	O									
ATOM	42	N	ASP	A	43	19.760	17.766	19.455	1.00	15.30
A	N									
ATOM	43	CA	ASP	A	43	21.130	17.962	19.902	1.00	13.64
A	C									
ATOM	44	CB	ASP	A	43	21.815	16.607	20.093	1.00	13.53
A	C									
ATOM	45	CG	ASP	A	43	23.177	16.732	20.753	1.00	18.06
A	C									
ATOM	46	OD1	ASP	A	43	24.185	16.931	20.042	1.00	15.90
A	O									
ATOM	47	OD2	ASP	A	43	23.235	16.645	21.993	1.00	20.18
A	O									
ATOM	48	C	ASP	A	43	21.869	18.802	18.855	1.00	12.61
A	C									
ATOM	49	O	ASP	A	43	21.634	18.661	17.655	1.00	12.49
A	O									
ATOM	50	N	LYS	A	44	22.755	19.682	19.303	1.00	11.01
A	N									
ATOM	51	CA	LYS	A	44	23.497	20.525	18.373	1.00	11.24
A	C									
ATOM	52	CB	LYS	A	44	24.368	21.536	19.129	1.00	11.63
A	C									
ATOM	53	CG	LYS	A	44	24.903	22.642	18.219	1.00	14.43
A	C									
ATOM	54	CD	LYS	A	44	25.657	23.738	18.977	1.00	16.69
A	C									



ATOM	55	CE	LYS	A	44	26.076	24.856	18.021	1.00	16.93
A	C									
ATOM	56	NZ	LYS	A	44	26.812	25.974	18.696	1.00	17.12
A	N									
ATOM	57	C	LYS	A	44	24.375	19.734	17.392	1.00	10.50
A	C									
ATOM	58	O	LYS	A	44	24.702	20.240	16.321	1.00	10.60
A	O									
ATOM	59	N	SER	A	45	24.753	18.507	17.745	1.00	8.11
A	N									
ATOM	60	CA	SER	A	45	25.585	17.699	16.844	1.00	10.59
A	C									
ATOM	61	CB	SER	A	45	25.941	16.352	17.479	1.00	10.95
A	C									
ATOM	62	OG	SER	A	45	24.779	15.624	17.827	1.00	12.31
A	O									
ATOM	63	C	SER	A	45	24.907	17.460	15.499	1.00	11.14
A	C									
ATOM	64	O	SER	A	45	25.571	17.208	14.496	1.00	10.24
A	O									
ATOM	65	N	ASN	A	46	23.582	17.533	15.477	1.00	10.77
A	N									
ATOM	66	CA	ASN	A	46	22.841	17.352	14.232	1.00	10.71
A	C									
ATOM	67	CB	ASN	A	46	21.335	17.486	14.476	1.00	10.57
A	C									
ATOM	68	CG	ASN	A	46	20.737	16.244	15.094	1.00	11.94
A	C									
ATOM	69	OD1	ASN	A	46	20.651	15.204	14.443	1.00	12.54
A	O									
ATOM	70	ND2	ASN	A	46	20.333	16.339	16.361	1.00	8.37
A	N									
ATOM	71	C	ASN	A	46	23.231	18.402	13.207	1.00	11.00
A	C									
ATOM	72	O	ASN	A	46	23.116	18.172	12.011	1.00	11.41
A	O									
ATOM	73	N	PHE	A	47	23.691	19.551	13.688	1.00	11.89
A	N									
ATOM	74	CA	PHE	A	47	24.028	20.671	12.812	1.00	13.43
A	C									
ATOM	75	CB	PHE	A	47	23.217	21.890	13.254	1.00	13.84
A	C									
ATOM	76	CG	PHE	A	47	21.760	21.593	13.463	1.00	13.84
A	C									
ATOM	77	CD1	PHE	A	47	20.886	21.510	12.377	1.00	15.85
A	C									
ATOM	78	CD2	PHE	A	47	21.273	21.347	14.739	1.00	12.02
A	C									
ATOM	79	CE1	PHE	A	47	19.543	21.182	12.567	1.00	15.39
A	C									
ATOM	80	CE2	PHE	A	47	19.937	21.019	14.940	1.00	14.91
A	C									
ATOM	81	CZ	PHE	A	47	19.068	20.935	13.855	1.00	12.76
A	C									
ATOM	82	C	PHE	A	47	25.498	21.047	12.773	1.00	12.62
A	C									
ATOM	83	O	PHE	A	47	25.846	22.136	12.312	1.00	13.52
A	O									

ATOM	84	N	GLN	A	48	26.361	20.152	13.243	1.00	13.34
A	N									
ATOM	85	CA	GLN	A	48	27.789	20.436	13.281	1.00	12.80
A	C									
ATOM	86	CB	GLN	A	48	28.300	20.324	14.719	1.00	12.87
A	C									
ATOM	87	CG	GLN	A	48	27.678	21.326	15.686	1.00	14.56
A	C									
ATOM	88	CD	GLN	A	48	28.082	21.066	17.116	1.00	16.25
A	C									
ATOM	89	OE1	GLN	A	48	27.892	19.965	17.634	1.00	18.12
A	O									
ATOM	90	NE2	GLN	A	48	28.644	22.075	17.766	1.00	15.04
A	N									
ATOM	91	C	GLN	A	48	28.636	19.542	12.388	1.00	14.54
A	C									
ATOM	92	O	GLN	A	48	29.860	19.568	12.486	1.00	13.57
A	O									
ATOM	93	N	GLN	A	49	27.998	18.749	11.528	1.00	12.16
A	N									
ATOM	94	CA	GLN	A	49	28.742	17.858	10.640	1.00	12.52
A	C									
ATOM	95	CB	GLN	A	49	27.990	16.530	10.503	1.00	12.58
A	C									
ATOM	96	CG	GLN	A	49	27.439	16.022	11.847	1.00	12.67
A	C									
ATOM	97	CD	GLN	A	49	28.483	16.019	12.961	1.00	15.57
A	C									
ATOM	98	OE1	GLN	A	49	29.730	15.772	12.598	1.00	12.50
A	O									
ATOM	99	NE2	GLN	A	49	28.165	16.234	14.136	1.00	14.24
A	N									
ATOM	100	C	GLN	A	49	28.941	18.568	9.295	1.00	12.85
A	C									
ATOM	101	O	GLN	A	49	27.985	18.899	8.589	1.00	11.22
A	O									
ATOM	102	N	PRO	A	50	30.204	18.823	8.927	1.00	13.42
A	N									
ATOM	103	CD	PRO	A	50	31.449	18.453	9.628	1.00	12.27
A	C									
ATOM	104	CA	PRO	A	50	30.492	19.514	7.666	1.00	12.60
A	C									
ATOM	105	CB	PRO	A	50	32.022	19.622	7.663	1.00	11.32
A	C									
ATOM	106	CG	PRO	A	50	32.460	18.448	8.495	1.00	14.19
A	C									
ATOM	107	C	PRO	A	50	29.948	18.944	6.370	1.00	11.49
A	C									
ATOM	108	O	PRO	A	50	29.464	19.697	5.520	1.00	10.14
A	O									
ATOM	109	N	TYR	A	51	30.001	17.629	6.205	1.00	11.00
A	N									
ATOM	110	CA	TYR	A	51	29.530	17.056	4.955	1.00	12.96
A	C									
ATOM	111	CB	TYR	A	51	29.750	15.535	4.932	1.00	14.28
A	C									
ATOM	112	CG	TYR	A	51	29.310	14.977	3.603	1.00	16.43
A	C									

ATOM	113	CD1	TYR	A	51	30.152	15.062	2.498	1.00	16.36
A	C									
ATOM	114	CE1	TYR	A	51	29.742	14.584	1.244	1.00	18.58
A	C									
ATOM	115	CD2	TYR	A	51	28.041	14.386	3.425	1.00	17.28
A	C									
ATOM	116	CE2	TYR	A	51	27.619	13.935	2.175	1.00	17.57
A	C									
ATOM	117	CZ	TYR	A	51	28.476	14.041	1.089	1.00	19.05
A	C									
ATOM	118	OH	TYR	A	51	28.068	13.623	-0.157	1.00	20.18
A	O									
ATOM	119	C	TYR	A	51	28.068	17.375	4.634	1.00	11.00
A	C									
ATOM	120	O	TYR	A	51	27.773	17.999	3.612	1.00	12.39
A	O									
ATOM	121	N	ILE	A	52	27.159	16.938	5.494	1.00	10.51
A	N									
ATOM	122	CA	ILE	A	52	25.746	17.175	5.222	1.00	10.19
A	C									
ATOM	123	CB	ILE	A	52	24.838	16.307	6.125	1.00	7.95
A	C									
ATOM	124	CG2	ILE	A	52	24.850	16.814	7.558	1.00	7.43
A	C									
ATOM	125	CG1	ILE	A	52	23.427	16.282	5.537	1.00	9.73
A	C									
ATOM	126	CD	ILE	A	52	23.341	15.576	4.193	1.00	9.58
A	C									
ATOM	127	C	ILE	A	52	25.351	18.640	5.335	1.00	9.53
A	C									
ATOM	128	O	ILE	A	52	24.416	19.073	4.671	1.00	10.79
A	O									
ATOM	129	N	THR	A	53	26.053	19.407	6.167	1.00	10.80
A	N									
ATOM	130	CA	THR	A	53	25.739	20.828	6.293	1.00	9.84
A	C									
ATOM	131	CB	THR	A	53	26.507	21.481	7.459	1.00	11.16
A	C									
ATOM	132	OG1	THR	A	53	26.155	20.833	8.690	1.00	12.87
A	O									
ATOM	133	CG2	THR	A	53	26.163	22.967	7.554	1.00	9.20
A	C									
ATOM	134	C	THR	A	53	26.126	21.519	4.977	1.00	11.45
A	C									
ATOM	135	O	THR	A	53	25.410	22.387	4.479	1.00	11.63
A	O									
ATOM	136	N	ASN	A	54	27.257	21.114	4.407	1.00	13.24
A	N									
ATOM	137	CA	ASN	A	54	27.708	21.691	3.141	1.00	13.84
A	C									
ATOM	138	CB	ASN	A	54	29.105	21.170	2.785	1.00	14.48
A	C									
ATOM	139	CG	ASN	A	54	29.639	21.771	1.500	1.00	14.91
A	C									
ATOM	140	OD1	ASN	A	54	29.687	22.986	1.348	1.00	18.44
A	O									
ATOM	141	ND2	ASN	A	54	30.045	20.920	0.571	1.00	19.20
A	N									

ATOM	142	C	ASN	A	54	26.719	21.350	2.025	1.00	12.10
A	C									
ATOM	143	O	ASN	A	54	26.380	22.200	1.205	1.00	13.81
A	O									
ATOM	144	N	ARG	A	55	26.260	20.102	1.997	1.00	14.14
A	N									
ATOM	145	CA	ARG	A	55	25.290	19.664	0.994	1.00	13.41
A	C									
ATOM	146	CB	ARG	A	55	24.950	18.180	1.176	1.00	15.87
A	C									
ATOM	147	CG	ARG	A	55	26.059	17.196	0.801	1.00	19.73
A	C									
ATOM	148	CD	ARG	A	55	26.505	17.386	-0.642	1.00	23.68
A	C									
ATOM	149	NE	ARG	A	55	27.405	16.325	-1.085	1.00	25.59
A	N									
ATOM	150	CZ	ARG	A	55	28.442	16.519	-1.891	1.00	27.42
A	C									
ATOM	151	NH1	ARG	A	55	28.710	17.733	-2.343	1.00	28.76
A	N									
ATOM	152	NH2	ARG	A	55	29.216	15.503	-2.241	1.00	27.48
A	N									
ATOM	153	C	ARG	A	55	24.007	20.480	1.129	1.00	11.99
A	C									
ATOM	154	O	ARG	A	55	23.412	20.893	0.134	1.00	11.77
A	O									
ATOM	155	N	THR	A	56	23.575	20.701	2.367	1.00	12.12
A	N									
ATOM	156	CA	THR	A	56	22.357	21.464	2.605	1.00	10.35
A	C									
ATOM	157	CB	THR	A	56	22.017	21.513	4.104	1.00	12.01
A	C									
ATOM	158	OG1	THR	A	56	21.792	20.180	4.591	1.00	7.11
A	O									
ATOM	159	CG2	THR	A	56	20.766	22.340	4.337	1.00	8.42
A	C									
ATOM	160	C	THR	A	56	22.483	22.889	2.062	1.00	12.24
A	C									
ATOM	161	O	THR	A	56	21.604	23.370	1.345	1.00	8.45
A	O									
ATOM	162	N	PHE	A	57	23.571	23.573	2.399	1.00	11.55
A	N									
ATOM	163	CA	PHE	A	57	23.753	24.937	1.914	1.00	12.54
A	C									
ATOM	164	CB	PHE	A	57	24.929	25.609	2.624	1.00	12.16
A	C									
ATOM	165	CG	PHE	A	57	24.568	26.181	3.960	1.00	13.36
A	C									
ATOM	166	CD1	PHE	A	57	24.313	25.354	5.046	1.00	13.15
A	C									
ATOM	167	CD2	PHE	A	57	24.464	27.553	4.130	1.00	14.39
A	C									
ATOM	168	CE1	PHE	A	57	23.961	25.887	6.282	1.00	14.05
A	C									
ATOM	169	CE2	PHE	A	57	24.113	28.092	5.359	1.00	12.06
A	C									
ATOM	170	CZ	PHE	A	57	23.862	27.259	6.438	1.00	13.80
A	C									

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ATOM	171	C	PHE	A	57	23.936	25.003	0.398	1.00	13.58
A	C									
ATOM	172	O	PHE	A	57	23.483	25.952	-0.244	1.00	13.09
A	O									
ATOM	173	N	MET	A	58	24.579	23.992	-0.177	1.00	13.90
A	N									
ATOM	174	CA	MET	A	58	24.782	23.969	-1.622	1.00	15.62
A	C									
ATOM	175	CB	MET	A	58	25.750	22.859	-2.019	1.00	16.17
A	C									
ATOM	176	CG	MET	A	58	27.164	23.047	-1.506	1.00	21.09
A	C									
ATOM	177	SD	MET	A	58	28.342	21.989	-2.379	1.00	27.56
A	S									
ATOM	178	CE	MET	A	58	27.683	20.368	-2.012	1.00	26.89
A	C									
ATOM	179	C	MET	A	58	23.454	23.759	-2.337	1.00	13.03
A	C									
ATOM	180	O	MET	A	58	23.215	24.322	-3.405	1.00	11.50
A	O									
ATOM	181	N	LEU	A	59	22.589	22.940	-1.749	1.00	12.01
A	N									
ATOM	182	CA	LEU	A	59	21.286	22.696	-2.347	1.00	12.06
A	C									
ATOM	183	CB	LEU	A	59	20.548	21.587	-1.597	1.00	12.51
A	C									
ATOM	184	CG	LEU	A	59	19.085	21.390	-2.012	1.00	13.80
A	C									
ATOM	185	CD1	LEU	A	59	18.991	21.124	-3.512	1.00	14.82
A	C									
ATOM	186	CD2	LEU	A	59	18.486	20.243	-1.225	1.00	10.84
A	C									
ATOM	187	C	LEU	A	59	20.474	23.990	-2.307	1.00	14.49
A	C									
ATOM	188	O	LEU	A	59	19.769	24.325	-3.262	1.00	13.13
A	O									
ATOM	189	N	ALA	A	60	20.578	24.718	-1.195	1.00	14.81
A	N									
ATOM	190	CA	ALA	A	60	19.857	25.974	-1.046	1.00	14.10
A	C									
ATOM	191	CB	ALA	A	60	20.077	26.545	0.344	1.00	14.30
A	C									
ATOM	192	C	ALA	A	60	20.339	26.963	-2.100	1.00	15.08
A	C									
ATOM	193	O	ALA	A	60	19.537	27.621	-2.761	1.00	12.89
A	O									
ATOM	194	N	LYS	A	61	21.654	27.065	-2.263	1.00	14.92
A	N									
ATOM	195	CA	LYS	A	61	22.209	27.985	-3.246	1.00	14.74
A	C									
ATOM	196	CB	LYS	A	61	23.740	27.926	-3.227	1.00	16.05
A	C									
ATOM	197	CG	LYS	A	61	24.421	28.890	-4.194	1.00	17.02
A	C									
ATOM	198	CD	LYS	A	61	24.047	30.325	-3.891	1.00	19.86
A	C									
ATOM	199	CE	LYS	A	61	24.717	31.288	-4.854	1.00	24.25
A	C									

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ATOM	200	NZ	LYS	A	61	24.367	32.697	-4.518	1.00	25.65
A	N									
ATOM	201	C	LYS	A	61	21.687	27.665	-4.642	1.00	15.27
A	C									
ATOM	202	O	LYS	A	61	21.161	28.537	-5.328	1.00	14.82
A	O									
ATOM	203	N	GLU	A	62	21.819	26.411	-5.057	1.00	15.81
A	N									
ATOM	204	CA	GLU	A	62	21.353	26.001	-6.373	1.00	18.42
A	C									
ATOM	205	CB	GLU	A	62	21.572	24.498	-6.555	1.00	20.56
A	C									
ATOM	206	CG	GLU	A	62	21.338	24.016	-7.969	1.00	27.23
A	C									
ATOM	207	CD	GLU	A	62	21.791	22.573	-8.214	1.00	31.47
A	C									
ATOM	208	OE1	GLU	A	62	22.875	22.136	-7.748	1.00	32.95
A	O									
ATOM	209	OE2	GLU	A	62	21.044	21.870	-8.914	1.00	33.23
A	O									
ATOM	210	C	GLU	A	62	19.879	26.348	-6.592	1.00	17.89
A	C									
ATOM	211	O	GLU	A	62	19.514	26.908	-7.625	1.00	16.93
A	O									
ATOM	212	N	ALA	A	63	19.029	26.021	-5.623	1.00	17.26
A	N									
ATOM	213	CA	ALA	A	63	17.605	26.316	-5.752	1.00	16.93
A	C									
ATOM	214	CB	ALA	A	63	16.832	25.692	-4.598	1.00	16.38
A	C									
ATOM	215	C	ALA	A	63	17.341	27.818	-5.801	1.00	17.17
A	C									
ATOM	216	O	ALA	A	63	16.477	28.280	-6.552	1.00	16.33
A	O									
ATOM	217	N	SER	A	64	18.079	28.586	-5.006	1.00	15.83
A	N									
ATOM	218	CA	SER	A	64	17.876	30.026	-4.992	1.00	18.51
A	C									
ATOM	219	CB	SER	A	64	18.748	30.686	-3.918	1.00	19.42
A	C									
ATOM	220	OG	SER	A	64	20.118	30.643	-4.267	1.00	21.79
A	O									
ATOM	221	C	SER	A	64	18.187	30.625	-6.364	1.00	19.15
A	C									
ATOM	222	O	SER	A	64	17.632	31.659	-6.739	1.00	18.21
A	O									
ATOM	223	N	LEU	A	65	19.067	29.966	-7.116	1.00	20.27
A	N									
ATOM	224	CA	LEU	A	65	19.433	30.454	-8.442	1.00	19.37
A	C									
ATOM	225	CB	LEU	A	65	20.727	29.797	-8.924	1.00	19.96
A	C									
ATOM	226	CG	LEU	A	65	22.002	30.321	-8.250	1.00	20.32
A	C									
ATOM	227	CD1	LEU	A	65	23.174	29.425	-8.604	1.00	21.39
A	C									
ATOM	228	CD2	LEU	A	65	22.268	31.752	-8.694	1.00	19.85
A	C									

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ATOM	229	C	LEU	A	65	18.317	30.182	-9.429	1.00	20.47
A	C									
ATOM	230	O	LEU	A	65	18.318	30.707	-10.545	1.00	19.18
A	O									
ATOM	231	N	ALA	A	66	17.363	29.358	-9.010	1.00	18.96
A	N									
ATOM	232	CA	ALA	A	66	16.231	29.022	-9.859	1.00	20.12
A	C									
ATOM	233	CB	ALA	A	66	15.983	27.521	-9.822	1.00	19.46
A	C									
ATOM	234	C	ALA	A	66	14.989	29.775	-9.390	1.00	21.39
A	C									
ATOM	235	O	ALA	A	66	13.926	29.661	-9.985	1.00	20.75
A	O									
ATOM	236	N	ASP	A	67	15.141	30.560	-8.331	1.00	22.23
A	N									
ATOM	237	CA	ASP	A	67	14.036	31.320	-7.761	1.00	24.31
A	C									
ATOM	238	CB	ASP	A	67	14.022	31.084	-6.246	1.00	25.00
A	C									
ATOM	239	CG	ASP	A	67	13.134	32.055	-5.497	1.00	24.66
A	C									
ATOM	240	OD1	ASP	A	67	12.112	32.513	-6.056	1.00	24.92
A	O									
ATOM	241	OD2	ASP	A	67	13.465	32.341	-4.328	1.00	21.55
A	O									
ATOM	242	C	ASP	A	67	14.116	32.813	-8.083	1.00	25.59
A	C									
ATOM	243	O	ASP	A	67	15.012	33.511	-7.609	1.00	25.98
A	O									
ATOM	244	N	ASN	A	68	13.172	33.297	-8.889	1.00	27.63
A	N									
ATOM	245	CA	ASN	A	68	13.138	34.708	-9.271	1.00	30.16
A	C									
ATOM	246	CB	ASN	A	68	12.696	34.857	-10.731	1.00	32.04
A	C									
ATOM	247	CG	ASN	A	68	13.815	34.567	-11.710	1.00	35.26
A	C									
ATOM	248	OD1	ASN	A	68	14.891	35.160	-11.627	1.00	37.18
A	O									
ATOM	249	ND2	ASN	A	68	13.567	33.661	-12.651	1.00	36.56
A	N									
ATOM	250	C	ASN	A	68	12.245	35.585	-8.401	1.00	31.73
A	C									
ATOM	251	O	ASN	A	68	12.134	36.785	-8.649	1.00	31.89
A	O									
ATOM	252	N	ASN	A	69	11.586	34.992	-7.408	1.00	32.78
A	N									
ATOM	253	CA	ASN	A	69	10.698	35.744	-6.519	1.00	35.19
A	C									
ATOM	254	CB	ASN	A	69	9.746	34.801	-5.772	1.00	36.74
A	C									
ATOM	255	CG	ASN	A	69	9.056	33.805	-6.688	1.00	40.93
A	C									
ATOM	256	OD1	ASN	A	69	8.300	34.186	-7.586	1.00	41.57
A	O									
ATOM	257	ND2	ASN	A	69	9.311	32.515	-6.461	1.00	40.68
A	N									

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ATOM	258	C	ASN	A	69	11.542	36.510	-5.501	1.00	35.09
A	C									
ATOM	259	O	ASN	A	69	11.646	36.109	-4.339	1.00	32.29
A	O									
ATOM	260	N	THR	A	70	12.134	37.615	-5.942	1.00	35.82
A	N									
ATOM	261	CA	THR	A	70	12.979	38.430	-5.078	1.00	37.87
A	C									
ATOM	262	CB	THR	A	70	13.852	39.386	-5.906	1.00	38.42
A	C									
ATOM	263	OG1	THR	A	70	13.014	40.346	-6.555	1.00	38.69
A	O									
ATOM	264	CG2	THR	A	70	14.631	38.623	-6.960	1.00	38.88
A	C									
ATOM	265	C	THR	A	70	12.192	39.275	-4.072	1.00	38.60
A	C									
ATOM	266	O	THR	A	70	12.781	39.904	-3.190	1.00	40.16
A	O									
ATOM	267	N	ASP	A	71	10.868	39.282	-4.196	1.00	39.04
A	N									
ATOM	268	CA	ASP	A	71	10.017	40.069	-3.305	1.00	39.32
A	C									
ATOM	269	CB	ASP	A	71	8.838	40.662	-4.078	1.00	42.61
A	C									
ATOM	270	CG	ASP	A	71	9.276	41.445	-5.281	1.00	47.01
A	C									
ATOM	271	OD1	ASP	A	71	9.915	40.831	-6.152	1.00	49.64
A	O									
ATOM	272	OD2	ASP	A	71	8.991	42.661	-5.362	1.00	50.35
A	O									
ATOM	273	C	ASP	A	71	9.451	39.301	-2.119	1.00	37.56
A	C									
ATOM	274	O	ASP	A	71	8.886	39.906	-1.206	1.00	37.36
A	O									
ATOM	275	N	VAL	A	72	9.590	37.979	-2.128	1.00	33.02
A	N									
ATOM	276	CA	VAL	A	72	9.040	37.171	-1.048	1.00	29.68
A	C									
ATOM	277	CB	VAL	A	72	8.003	36.165	-1.590	1.00	31.44
A	C									
ATOM	278	CG1	VAL	A	72	7.361	35.408	-0.437	1.00	31.76
A	C									
ATOM	279	CG2	VAL	A	72	6.951	36.899	-2.416	1.00	34.37
A	C									
ATOM	280	C	VAL	A	72	10.074	36.392	-0.252	1.00	26.18
A	C									
ATOM	281	O	VAL	A	72	11.011	35.825	-0.814	1.00	24.53
A	O									
ATOM	282	N	ARG	A	73	9.879	36.372	1.061	1.00	24.81
A	N									
ATOM	283	CA	ARG	A	73	10.744	35.656	1.996	1.00	25.04
A	C									
ATOM	284	CB	ARG	A	73	11.426	36.640	2.951	1.00	27.84
A	C									
ATOM	285	CG	ARG	A	73	12.237	35.992	4.066	1.00	31.02
A	C									
ATOM	286	CD	ARG	A	73	13.488	35.315	3.527	1.00	33.29
A	C									



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ATOM	287	NE	ARG	A	73	14.469	36.271	3.019	1.00	37.87
A	N									
ATOM	288	CZ	ARG	A	73	15.093	37.178	3.765	1.00	39.29
A	C									
ATOM	289	NH1	ARG	A	73	14.847	37.266	5.066	1.00	39.10
A	N									
ATOM	290	NH2	ARG	A	73	15.967	38.002	3.207	1.00	42.25
A	N									
ATOM	291	C	ARG	A	73	9.819	34.739	2.783	1.00	23.44
A	C									
ATOM	292	O	ARG	A	73	8.797	35.189	3.303	1.00	23.25
A	O									
ATOM	293	N	LEU	A	74	10.158	33.458	2.871	1.00	20.73
A	N									
ATOM	294	CA	LEU	A	74	9.311	32.522	3.602	1.00	18.25
A	C									
ATOM	295	CB	LEU	A	74	9.412	31.120	2.994	1.00	19.13
A	C									
ATOM	296	CG	LEU	A	74	8.937	30.973	1.546	1.00	19.57
A	C									
ATOM	297	CD1	LEU	A	74	9.020	29.523	1.122	1.00	19.10
A	C									
ATOM	298	CD2	LEU	A	74	7.504	31.462	1.420	1.00	19.94
A	C									
ATOM	299	C	LEU	A	74	9.655	32.466	5.081	1.00	18.81
A	C									
ATOM	300	O	LEU	A	74	8.772	32.562	5.930	1.00	17.72
A	O									
ATOM	301	N	ILE	A	75	10.940	32.307	5.391	1.00	17.09
A	N									
ATOM	302	CA	ILE	A	75	11.375	32.239	6.781	1.00	16.71
A	C									
ATOM	303	CB	ILE	A	75	12.503	31.195	6.948	1.00	17.07
A	C									
ATOM	304	CG2	ILE	A	75	13.077	31.258	8.361	1.00	17.86
A	C									
ATOM	305	CG1	ILE	A	75	11.950	29.798	6.642	1.00	18.78
A	C									
ATOM	306	CD	ILE	A	75	12.978	28.681	6.749	1.00	18.86
A	C									
ATOM	307	C	ILE	A	75	11.848	33.612	7.263	1.00	17.51
A	C									
ATOM	308	O	ILE	A	75	12.939	34.062	6.931	1.00	15.26
A	O									
ATOM	309	N	GLY	A	76	11.017	34.281	8.052	1.00	18.34
A	N									
ATOM	310	CA	GLY	A	76	11.389	35.600	8.530	1.00	21.35
A	C									
ATOM	311	C	GLY	A	76	10.608	36.007	9.761	1.00	23.15
A	C									
ATOM	312	O	GLY	A	76	9.916	35.187	10.357	1.00	21.36
A	O									
ATOM	313	N	GLU	A	77	10.706	37.282	10.125	1.00	26.14
A	N									
ATOM	314	CA	GLU	A	77	10.043	37.817	11.313	1.00	27.91
A	C									
ATOM	315	CB	GLU	A	77	10.118	39.349	11.300	1.00	31.26
A	C									

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ATOM	316	CG	GLU	A	77	9.551	40.011	12.548	1.00	36.17
A	C									
ATOM	317	CD	GLU	A	77	9.807	41.508	12.584	1.00	39.76
A	C									
ATOM	318	OE1	GLU	A	77	9.440	42.203	11.609	1.00	39.06
A	O									
ATOM	319	OE2	GLU	A	77	10.375	41.986	13.591	1.00	41.22
A	O									
ATOM	320	C	GLU	A	77	8.595	37.370	11.517	1.00	27.70
A	C									
ATOM	321	O	GLU	A	77	8.235	36.899	12.595	1.00	28.81
A	O									
ATOM	322	N	LYS	A	78	7.767	37.514	10.491	1.00	27.14
A	N									
ATOM	323	CA	LYS	A	78	6.364	37.125	10.594	1.00	26.90
A	C									
ATOM	324	CB	LYS	A	78	5.652	37.351	9.254	1.00	29.37
A	C									
ATOM	325	CG	LYS	A	78	6.481	36.998	8.023	1.00	34.70
A	C									
ATOM	326	CD	LYS	A	78	7.597	38.018	7.773	1.00	35.71
A	C									
ATOM	327	CE	LYS	A	78	8.457	37.619	6.584	1.00	37.67
A	C									
ATOM	328	NZ	LYS	A	78	9.458	38.670	6.251	1.00	39.35
A	N									
ATOM	329	C	LYS	A	78	6.147	35.688	11.061	1.00	24.99
A	C									
ATOM	330	O	LYS	A	78	5.244	35.419	11.850	1.00	24.73
A	O									
ATOM	331	N	LEU	A	79	6.974	34.765	10.580	1.00	23.10
A	N									
ATOM	332	CA	LEU	A	79	6.851	33.360	10.954	1.00	21.97
A	C									
ATOM	333	CB	LEU	A	79	7.903	32.533	10.206	1.00	21.38
A	C									
ATOM	334	CG	LEU	A	79	7.963	31.034	10.510	1.00	19.79
A	C									
ATOM	335	CD1	LEU	A	79	6.618	30.386	10.186	1.00	18.36
A	C									
ATOM	336	CD2	LEU	A	79	9.076	30.395	9.688	1.00	18.38
A	C									
ATOM	337	C	LEU	A	79	7.005	33.126	12.457	1.00	22.48
A	C									
ATOM	338	O	LEU	A	79	6.378	32.232	13.026	1.00	21.54
A	O									
ATOM	339	N	PHE	A	80	7.839	33.936	13.098	1.00	24.35
A	N									
ATOM	340	CA	PHE	A	80	8.102	33.799	14.525	1.00	25.81
A	C									
ATOM	341	CB	PHE	A	80	9.599	33.972	14.768	1.00	24.41
A	C									
ATOM	342	CG	PHE	A	80	10.447	33.009	13.990	1.00	24.03
A	C									
ATOM	343	CD1	PHE	A	80	10.510	31.667	14.351	1.00	23.62
A	C									
ATOM	344	CD2	PHE	A	80	11.158	33.437	12.875	1.00	23.15
A	C									

ATOM	345	CE1	PHE	A	80	11.270	30.759	13.606	1.00	23.39
A	C									
ATOM	346	CE2	PHE	A	80	11.917	32.543	12.125	1.00	23.09
A	C									
ATOM	347	CZ	PHE	A	80	11.974	31.200	12.491	1.00	23.28
A	C									
ATOM	348	C	PHE	A	80	7.324	34.775	15.410	1.00	28.55
A	C									
ATOM	349	O	PHE	A	80	7.362	34.676	16.637	1.00	28.74
A	O									
ATOM	350	N	HIS	A	81	6.618	35.711	14.787	1.00	30.56
A	N									
ATOM	351	CA	HIS	A	81	5.849	36.711	15.519	1.00	32.02
A	C									
ATOM	352	CB	HIS	A	81	5.051	37.579	14.540	1.00	34.06
A	C									
ATOM	353	CG	HIS	A	81	4.321	38.711	15.193	1.00	36.89
A	C									
ATOM	354	CD2	HIS	A	81	2.996	38.959	15.325	1.00	37.63
A	C									
ATOM	355	ND1	HIS	A	81	4.971	39.748	15.829	1.00	38.12
A	N									
ATOM	356	CE1	HIS	A	81	4.078	40.585	16.325	1.00	38.01
A	C									
ATOM	357	NE2	HIS	A	81	2.873	40.129	16.033	1.00	38.42
A	N									
ATOM	358	C	HIS	A	81	4.902	36.097	16.547	1.00	30.87
A	C									
ATOM	359	O	HIS	A	81	4.060	35.268	16.211	1.00	32.80
A	O									
ATOM	360	N	GLY	A	82	5.046	36.511	17.802	1.00	30.56
A	N									
ATOM	361	CA	GLY	A	82	4.192	35.997	18.859	1.00	29.32
A	C									
ATOM	362	C	GLY	A	82	4.593	34.640	19.420	1.00	28.91
A	C									
ATOM	363	O	GLY	A	82	3.989	34.165	20.380	1.00	29.61
A	O									
ATOM	364	N	VAL	A	83	5.609	34.011	18.835	1.00	26.58
A	N									
ATOM	365	CA	VAL	A	83	6.064	32.697	19.295	1.00	24.46
A	C									
ATOM	366	CB	VAL	A	83	6.569	31.855	18.096	1.00	24.84
A	C									
ATOM	367	CG1	VAL	A	83	6.971	30.470	18.531	1.00	24.49
A	C									
ATOM	368	CG2	VAL	A	83	5.480	31.749	17.066	1.00	24.95
A	C									
ATOM	369	C	VAL	A	83	7.180	32.847	20.328	1.00	23.20
A	C									
ATOM	370	O	VAL	A	83	8.218	33.429	20.043	1.00	20.58
A	O									
ATOM	371	N	SER	A	84	6.956	32.336	21.535	1.00	22.74
A	N									
ATOM	372	CA	SER	A	84	7.961	32.427	22.586	1.00	22.59
A	C									
ATOM	373	CB	SER	A	84	7.325	32.136	23.942	1.00	24.87
A	C									

ATOM	374	OG	SER	A	84	6.740	30.847	23.960	1.00	28.28
A	O									
ATOM	375	C	SER	A	84	9.091	31.438	22.319	1.00	22.22
A	C									
ATOM	376	O	SER	A	84	8.891	30.428	21.649	1.00	19.25
A	O									
ATOM	377	N	MET	A	85	10.271	31.723	22.860	1.00	22.89
A	N									
ATOM	378	CA	MET	A	85	11.438	30.864	22.661	1.00	23.51
A	C									
ATOM	379	CB	MET	A	85	12.626	31.391	23.470	1.00	26.40
A	C									
ATOM	380	CG	MET	A	85	12.965	32.850	23.205	1.00	32.22
A	C									
ATOM	381	SD	MET	A	85	13.130	33.234	21.443	1.00	38.24
A	S									
ATOM	382	CE	MET	A	85	11.634	34.156	21.178	1.00	39.11
A	C									
ATOM	383	C	MET	A	85	11.213	29.391	23.010	1.00	21.82
A	C									
ATOM	384	O	MET	A	85	11.799	28.506	22.387	1.00	21.96
A	O									
ATOM	385	N	SER	A	86	10.377	29.121	24.006	1.00	20.05
A	N									
ATOM	386	CA	SER	A	86	10.123	27.743	24.405	1.00	20.16
A	C									
ATOM	387	CB	SER	A	86	9.504	27.701	25.801	1.00	20.31
A	C									
ATOM	388	OG	SER	A	86	8.281	28.406	25.816	1.00	19.38
A	O									
ATOM	389	C	SER	A	86	9.215	26.993	23.436	1.00	20.16
A	C									
ATOM	390	O	SER	A	86	9.039	25.780	23.563	1.00	21.23
A	O									
ATOM	391	N	GLU	A	87	8.633	27.702	22.475	1.00	18.55
A	N									
ATOM	392	CA	GLU	A	87	7.757	27.044	21.505	1.00	19.19
A	C									
ATOM	393	CB	GLU	A	87	6.381	27.717	21.480	1.00	21.48
A	C									
ATOM	394	CG	GLU	A	87	5.848	28.071	22.849	1.00	27.63
A	C									
ATOM	395	CD	GLU	A	87	4.583	28.925	22.796	1.00	30.13
A	C									
ATOM	396	OE1	GLU	A	87	4.609	30.033	22.220	1.00	30.21
A	O									
ATOM	397	OE2	GLU	A	87	3.553	28.497	23.344	1.00	33.94
A	O									
ATOM	398	C	GLU	A	87	8.337	27.066	20.095	1.00	17.25
A	C									
ATOM	399	O	GLU	A	87	7.786	26.443	19.189	1.00	15.95
A	O									
ATOM	400	N	ARG	A	88	9.447	27.778	19.910	1.00	16.02
A	N									
ATOM	401	CA	ARG	A	88	10.081	27.887	18.599	1.00	15.63
A	C									
ATOM	402	CB	ARG	A	88	11.356	28.729	18.693	1.00	18.69
A	C									

ATOM	403	CG	ARG	A	88	11.146	30.190	19.067	1.00	23.67
A	C									
ATOM	404	CD	ARG	A	88	10.457	30.944	17.961	1.00	26.36
A	C									
ATOM	405	NE	ARG	A	88	10.175	32.337	18.311	1.00	30.28
A	N									
ATOM	406	CZ	ARG	A	88	11.044	33.337	18.206	1.00	31.77
A	C									
ATOM	407	NH1	ARG	A	88	12.270	33.111	17.762	1.00	34.62
A	N									
ATOM	408	NH2	ARG	A	88	10.678	34.574	18.518	1.00	30.69
A	N									
ATOM	409	C	ARG	A	88	10.423	26.541	17.951	1.00	15.43
A	C									
ATOM	410	O	ARG	A	88	10.153	26.333	16.767	1.00	15.17
A	O									
ATOM	411	N	CYS	A	89	11.025	25.628	18.708	1.00	12.14
A	N									
ATOM	412	CA	CYS	A	89	11.381	24.342	18.120	1.00	13.07
A	C									
ATOM	413	C	CYS	A	89	10.133	23.605	17.611	1.00	14.78
A	C									
ATOM	414	O	CYS	A	89	10.158	23.020	16.528	1.00	13.46
A	O									
ATOM	415	CB	CYS	A	89	12.169	23.472	19.107	1.00	12.57
A	C									
ATOM	416	SG	CYS	A	89	12.780	21.964	18.306	1.00	15.35
A	S									
ATOM	417	N	TYR	A	90	9.044	23.653	18.378	1.00	13.52
A	N									
ATOM	418	CA	TYR	A	90	7.789	23.017	17.970	1.00	14.36
A	C									
ATOM	419	CB	TYR	A	90	6.729	23.149	19.063	1.00	16.25
A	C									
ATOM	420	CG	TYR	A	90	5.386	22.598	18.640	1.00	20.73
A	C									
ATOM	421	CD1	TYR	A	90	5.172	21.220	18.551	1.00	22.84
A	C									
ATOM	422	CE1	TYR	A	90	3.936	20.704	18.142	1.00	25.51
A	C									
ATOM	423	CD2	TYR	A	90	4.334	23.453	18.308	1.00	21.97
A	C									
ATOM	424	CE2	TYR	A	90	3.095	22.947	17.894	1.00	25.27
A	C									
ATOM	425	CZ	TYR	A	90	2.908	21.575	17.813	1.00	26.64
A	C									
ATOM	426	OH	TYR	A	90	1.698	21.073	17.393	1.00	31.95
A	O									
ATOM	427	C	TYR	A	90	7.283	23.691	16.699	1.00	12.19
A	C									
ATOM	428	O	TYR	A	90	6.762	23.032	15.797	1.00	13.82
A	O									
ATOM	429	N	LEU	A	91	7.430	25.011	16.630	1.00	13.87
A	N									
ATOM	430	CA	LEU	A	91	7.020	25.763	15.445	1.00	14.25
A	C									
ATOM	431	CB	LEU	A	91	7.279	27.259	15.657	1.00	16.00
A	C									

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ATOM	432	CG	LEU	A	91	7.389	28.125	14.403	1.00	20.38
A	C									
ATOM	433	CD1	LEU	A	91	6.049	28.180	13.691	1.00	20.90
A	C									
ATOM	434	CD2	LEU	A	91	7.848	29.522	14.795	1.00	23.19
A	C									
ATOM	435	C	LEU	A	91	7.841	25.271	14.250	1.00	14.26
A	C									
ATOM	436	O	LEU	A	91	7.298	25.011	13.166	1.00	13.95
A	O									
ATOM	437	N	MET	A	92	9.156	25.144	14.454	1.00	13.32
A	N									
ATOM	438	CA	MET	A	92	10.054	24.693	13.386	1.00	12.34
A	C									
ATOM	439	CB	MET	A	92	11.520	24.855	13.791	1.00	13.46
A	C									
ATOM	440	CG	MET	A	92	11.943	26.329	13.855	1.00	13.93
A	C									
ATOM	441	SD	MET	A	92	11.513	27.272	12.365	1.00	19.44
A	S									
ATOM	442	CE	MET	A	92	12.398	26.314	11.091	1.00	16.94
A	C									
ATOM	443	C	MET	A	92	9.763	23.272	12.941	1.00	13.49
A	C									
ATOM	444	O	MET	A	92	9.975	22.924	11.777	1.00	14.17
A	O									
ATOM	445	N	LYS	A	93	9.255	22.465	13.864	1.00	12.98
A	N									
ATOM	446	CA	LYS	A	93	8.889	21.097	13.557	1.00	13.82
A	C									
ATOM	447	CB	LYS	A	93	8.385	20.395	14.810	1.00	13.12
A	C									
ATOM	448	CG	LYS	A	93	7.672	19.082	14.522	1.00	18.61
A	C									
ATOM	449	CD	LYS	A	93	6.889	18.604	15.736	1.00	18.28
A	C									
ATOM	450	CE	LYS	A	93	6.085	17.352	15.441	1.00	20.53
A	C									
ATOM	451	NZ	LYS	A	93	5.352	16.889	16.657	1.00	19.33
A	N									
ATOM	452	C	LYS	A	93	7.770	21.124	12.526	1.00	13.87
A	C									
ATOM	453	O	LYS	A	93	7.760	20.328	11.593	1.00	15.68
A	O									
ATOM	454	N	GLN	A	94	6.823	22.043	12.700	1.00	15.16
A	N									
ATOM	455	CA	GLN	A	94	5.692	22.144	11.778	1.00	15.15
A	C									
ATOM	456	CB	GLN	A	94	4.630	23.089	12.344	1.00	17.59
A	C									
ATOM	457	CG	GLN	A	94	4.254	22.779	13.786	1.00	23.02
A	C									
ATOM	458	CD	GLN	A	94	3.713	21.376	13.964	1.00	25.41
A	C									
ATOM	459	OE1	GLN	A	94	3.829	20.788	15.038	1.00	31.14
A	O									
ATOM	460	NE2	GLN	A	94	3.110	20.836	12.917	1.00	25.01
A	N									

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ATOM	461	C	GLN	A	94	6.157	22.644	10.419	1.00	13.97
A	C									
ATOM	462	O	GLN	A	94	5.687	22.179	9.378	1.00	13.38
A	O									
ATOM	463	N	VAL	A	95	7.082	23.599	10.429	1.00	12.42
A	N									
ATOM	464	CA	VAL	A	95	7.598	24.140	9.183	1.00	11.71
A	C									
ATOM	465	CB	VAL	A	95	8.539	25.324	9.420	1.00	12.14
A	C									
ATOM	466	CG1	VAL	A	95	9.180	25.740	8.107	1.00	13.43
A	C									
ATOM	467	CG2	VAL	A	95	7.767	26.483	9.997	1.00	12.64
A	C									
ATOM	468	C	VAL	A	95	8.373	23.060	8.452	1.00	12.55
A	C									
ATOM	469	O	VAL	A	95	8.269	22.930	7.232	1.00	10.70
A	O									
ATOM	470	N	LEU	A	96	9.150	22.287	9.210	1.00	11.35
A	N									
ATOM	471	CA	LEU	A	96	9.953	21.212	8.639	1.00	9.86
A	C									
ATOM	472	CB	LEU	A	96	10.822	20.559	9.712	1.00	10.52
A	C									
ATOM	473	CG	LEU	A	96	11.572	19.302	9.248	1.00	12.76
A	C									
ATOM	474	CD1	LEU	A	96	12.575	19.657	8.158	1.00	11.47
A	C									
ATOM	475	CD2	LEU	A	96	12.282	18.662	10.445	1.00	11.92
A	C									
ATOM	476	C	LEU	A	96	9.088	20.145	7.994	1.00	10.33
A	C									
ATOM	477	O	LEU	A	96	9.327	19.751	6.855	1.00	10.88
A	O									
ATOM	478	N	ASN	A	97	8.086	19.669	8.725	1.00	11.10
A	N									
ATOM	479	CA	ASN	A	97	7.215	18.630	8.192	1.00	12.58
A	C									
ATOM	480	CB	ASN	A	97	6.270	18.130	9.290	1.00	15.76
A	C									
ATOM	481	CG	ASN	A	97	7.013	17.361	10.377	1.00	16.70
A	C									
ATOM	482	OD1	ASN	A	97	8.146	16.920	10.168	1.00	19.35
A	O									
ATOM	483	ND2	ASN	A	97	6.380	17.182	11.525	1.00	17.01
A	N									
ATOM	484	C	ASN	A	97	6.462	19.114	6.964	1.00	11.81
A	C									
ATOM	485	O	ASN	A	97	6.281	18.361	6.006	1.00	12.10
A	O									
ATOM	486	N	PHE	A	98	6.037	20.374	6.971	1.00	12.85
A	N									
ATOM	487	CA	PHE	A	98	5.347	20.917	5.806	1.00	13.45
A	C									
ATOM	488	CB	PHE	A	98	4.907	22.357	6.052	1.00	14.09
A	C									
ATOM	489	CG	PHE	A	98	4.623	23.121	4.788	1.00	17.24
A	C									

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ATOM	490	CD1	PHE	A	98	3.535	22.793	3.986	1.00	18.81
A	C									
ATOM	491	CD2	PHE	A	98	5.472	24.141	4.378	1.00	18.95
A	C									
ATOM	492	CE1	PHE	A	98	3.301	23.469	2.790	1.00	19.48
A	C									
ATOM	493	CE2	PHE	A	98	5.247	24.820	3.188	1.00	18.82
A	C									
ATOM	494	CZ	PHE	A	98	4.163	24.484	2.392	1.00	18.93
A	C									
ATOM	495	C	PHE	A	98	6.316	20.906	4.629	1.00	13.98
A	C									
ATOM	496	O	PHE	A	98	5.991	20.458	3.519	1.00	12.54
A	O									
ATOM	497	N	THR	A	99	7.519	21.405	4.878	1.00	12.46
A	N									
ATOM	498	CA	THR	A	99	8.509	21.473	3.818	1.00	12.12
A	C									
ATOM	499	CB	THR	A	99	9.789	22.174	4.297	1.00	13.25
A	C									
ATOM	500	OG1	THR	A	99	9.459	23.469	4.825	1.00	11.71
A	O									
ATOM	501	CG2	THR	A	99	10.745	22.345	3.137	1.00	12.11
A	C									
ATOM	502	C	THR	A	99	8.852	20.099	3.260	1.00	11.68
A	C									
ATOM	503	O	THR	A	99	9.081	19.950	2.061	1.00	12.57
A	O									
ATOM	504	N	LEU	A	100	8.892	19.092	4.124	1.00	12.47
A	N									
ATOM	505	CA	LEU	A	100	9.189	17.741	3.668	1.00	13.58
A	C									
ATOM	506	CB	LEU	A	100	9.405	16.817	4.870	1.00	13.64
A	C									
ATOM	507	CG	LEU	A	100	10.794	16.844	5.519	1.00	14.13
A	C									
ATOM	508	CD1	LEU	A	100	10.766	16.117	6.859	1.00	15.07
A	C									
ATOM	509	CD2	LEU	A	100	11.788	16.191	4.583	1.00	11.06
A	C									
ATOM	510	C	LEU	A	100	8.056	17.179	2.802	1.00	15.63
A	C									
ATOM	511	O	LEU	A	100	8.285	16.726	1.684	1.00	14.71
A	O									
ATOM	512	N	GLU	A	101	6.838	17.223	3.332	1.00	15.43
A	N									
ATOM	513	CA	GLU	A	101	5.660	16.687	2.656	1.00	17.18
A	C									
ATOM	514	CB	GLU	A	101	4.467	16.670	3.618	1.00	18.69
A	C									
ATOM	515	CG	GLU	A	101	4.530	15.627	4.730	1.00	22.02
A	C									
ATOM	516	CD	GLU	A	101	4.465	14.207	4.212	1.00	26.32
A	C									
ATOM	517	OE1	GLU	A	101	3.657	13.940	3.299	1.00	27.27
A	O									
ATOM	518	OE2	GLU	A	101	5.212	13.344	4.724	1.00	29.94
A	O									

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ATOM	519	C	GLU A 101	5.220	17.375	1.370	1.00	17.32
A	C							
ATOM	520	O	GLU A 101	4.913	16.706	0.378	1.00	17.41
A	O							
ATOM	521	N	GLU A 102	5.194	18.702	1.378	1.00	16.65
A	N							
ATOM	522	CA	GLU A 102	4.725	19.442	0.212	1.00	16.41
A	C							
ATOM	523	CB	GLU A 102	3.629	20.402	0.657	1.00	19.20
A	C							
ATOM	524	CG	GLU A 102	2.440	19.644	1.233	1.00	23.30
A	C							
ATOM	525	CD	GLU A 102	1.369	20.554	1.771	1.00	26.38
A	C							
ATOM	526	OE1	GLU A 102	0.828	21.357	0.981	1.00	25.51
A	O							
ATOM	527	OE2	GLU A 102	1.073	20.465	2.984	1.00	27.95
A	O							
ATOM	528	C	GLU A 102	5.745	20.170	-0.650	1.00	16.28
A	C							
ATOM	529	O	GLU A 102	5.385	20.783	-1.653	1.00	14.86
A	O							
ATOM	530	N	VAL A 103	7.015	20.109	-0.271	1.00	12.43
A	N							
ATOM	531	CA	VAL A 103	8.045	20.755	-1.077	1.00	13.07
A	C							
ATOM	532	CB	VAL A 103	8.742	21.907	-0.320	1.00	12.76
A	C							
ATOM	533	CG1	VAL A 103	9.889	22.458	-1.162	1.00	12.19
A	C							
ATOM	534	CG2	VAL A 103	7.753	23.024	-0.027	1.00	13.33
A	C							
ATOM	535	C	VAL A 103	9.122	19.763	-1.509	1.00	13.14
A	C							
ATOM	536	O	VAL A 103	9.271	19.462	-2.690	1.00	13.73
A	O							
ATOM	537	N	LEU A 104	9.863	19.248	-0.538	1.00	12.65
A	N							
ATOM	538	CA	LEU A 104	10.952	18.330	-0.824	1.00	14.40
A	C							
ATOM	539	CB	LEU A 104	11.785	18.113	0.441	1.00	14.50
A	C							
ATOM	540	CG	LEU A 104	12.438	19.396	0.972	1.00	14.36
A	C							
ATOM	541	CD1	LEU A 104	13.126	19.115	2.295	1.00	15.72
A	C							
ATOM	542	CD2	LEU A 104	13.441	19.928	-0.050	1.00	14.39
A	C							
ATOM	543	C	LEU A 104	10.544	16.989	-1.415	1.00	15.37
A	C							
ATOM	544	O	LEU A 104	11.215	16.480	-2.313	1.00	12.81
A	O							
ATOM	545	N	PHE A 105	9.467	16.399	-0.916	1.00	15.46
A	N							
ATOM	546	CA	PHE A 105	9.054	15.115	-1.466	1.00	17.77
A	C							
ATOM	547	CB	PHE A 105	7.926	14.508	-0.621	1.00	18.57
A	C							

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ATOM	548	CG	PHE A 105	8.400	13.952	0.706	1.00	20.35
A	C							
ATOM	549	CD1	PHE A 105	9.750	14.016	1.066	1.00	22.06
A	C							
ATOM	550	CD2	PHE A 105	7.505	13.366	1.590	1.00	21.24
A	C							
ATOM	551	CE1	PHE A 105	10.193	13.501	2.288	1.00	22.72
A	C							
ATOM	552	CE2	PHE A 105	7.935	12.847	2.817	1.00	21.30
A	C							
ATOM	553	CZ	PHE A 105	9.280	12.914	3.168	1.00	24.04
A	C							
ATOM	554	C	PHE A 105	8.658	15.282	-2.935	1.00	17.82
A	C							
ATOM	555	O	PHE A 105	9.150	14.549	-3.798	1.00	17.32
A	O							
ATOM	556	N	PRO A 106	7.788	16.263	-3.244	1.00	19.25
A	N							
ATOM	557	CD	PRO A 106	6.995	17.100	-2.323	1.00	18.44
A	C							
ATOM	558	CA	PRO A 106	7.372	16.487	-4.634	1.00	19.95
A	C							
ATOM	559	CB	PRO A 106	6.417	17.672	-4.521	1.00	20.31
A	C							
ATOM	560	CG	PRO A 106	5.806	17.480	-3.174	1.00	19.88
A	C							
ATOM	561	C	PRO A 106	8.563	16.800	-5.541	1.00	20.82
A	C							
ATOM	562	O	PRO A 106	8.553	16.483	-6.734	1.00	19.57
A	O							
ATOM	563	N	GLN A 107	9.593	17.417	-4.964	1.00	21.36
A	N							
ATOM	564	CA	GLN A 107	10.791	17.800	-5.714	1.00	21.96
A	C							
ATOM	565	CB	GLN A 107	11.198	19.233	-5.335	1.00	22.81
A	C							
ATOM	566	CG	GLN A 107	10.156	20.298	-5.638	1.00	24.02
A	C							
ATOM	567	CD	GLN A 107	10.184	20.735	-7.086	1.00	27.15
A	C							
ATOM	568	OE1	GLN A 107	9.302	21.459	-7.547	1.00	28.19
A	O							
ATOM	569	NE2	GLN A 107	11.211	20.306	-7.811	1.00	27.09
A	N							
ATOM	570	C	GLN A 107	11.968	16.872	-5.438	1.00	22.05
A	C							
ATOM	571	O	GLN A 107	13.090	17.145	-5.871	1.00	21.11
A	O							
ATOM	572	N	SER A 108	11.709	15.773	-4.734	1.00	22.40
A	N							
ATOM	573	CA	SER A 108	12.756	14.829	-4.342	1.00	24.12
A	C							
ATOM	574	CB	SER A 108	12.142	13.665	-3.559	1.00	21.76
A	C							
ATOM	575	OG	SER A 108	11.263	12.909	-4.370	1.00	25.11
A	O							
ATOM	576	C	SER A 108	13.667	14.276	-5.434	1.00	25.68
A	C							

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ATOM	577	O	SER A 108	14.823	13.942	-5.168	1.00	25.48
A	O							
ATOM	578	N	ASP A 109	13.165	14.179	-6.658	1.00	28.58
A	N							
ATOM	579	CA	ASP A 109	13.976	13.654	-7.750	1.00	29.53
A	C							
ATOM	580	CB	ASP A 109	13.131	12.719	-8.623	1.00	31.30
A	C							
ATOM	581	CG	ASP A 109	11.897	13.398	-9.189	1.00	33.47
A	C							
ATOM	582	OD1	ASP A 109	11.371	14.328	-8.542	1.00	33.88
A	O							
ATOM	583	OD2	ASP A 109	11.443	12.987	-10.278	1.00	33.45
A	O							
ATOM	584	C	ASP A 109	14.587	14.765	-8.593	1.00	30.64
A	C							
ATOM	585	O	ASP A 109	15.058	14.527	-9.706	1.00	32.81
A	O							
ATOM	586	N	ARG A 110	14.592	15.979	-8.050	1.00	29.79
A	N							
ATOM	587	CA	ARG A 110	15.145	17.134	-8.748	1.00	28.46
A	C							
ATOM	588	CB	ARG A 110	14.107	18.251	-8.819	1.00	31.87
A	C							
ATOM	589	CG	ARG A 110	14.497	19.382	-9.753	1.00	37.18
A	C							
ATOM	590	CD	ARG A 110	13.655	19.374	-11.020	1.00	41.24
A	C							
ATOM	591	NE	ARG A 110	12.340	19.974	-10.803	1.00	43.98
A	N							
ATOM	592	CZ	ARG A 110	12.146	21.255	-10.497	1.00	44.48
A	C							
ATOM	593	NH1	ARG A 110	13.180	22.074	-10.373	1.00	44.65
A	N							
ATOM	594	NH2	ARG A 110	10.916	21.718	-10.315	1.00	45.63
A	N							
ATOM	595	C	ARG A 110	16.384	17.629	-8.008	1.00	25.45
A	C							
ATOM	596	O	ARG A 110	16.715	17.118	-6.942	1.00	25.04
A	O							
ATOM	597	N	PHE A 111	17.070	18.616	-8.576	1.00	22.98
A	N							
ATOM	598	CA	PHE A 111	18.278	19.163	-7.965	1.00	22.26
A	C							
ATOM	599	CB	PHE A 111	17.900	20.022	-6.749	1.00	21.90
A	C							
ATOM	600	CG	PHE A 111	17.148	21.274	-7.111	1.00	18.30
A	C							
ATOM	601	CD1	PHE A 111	17.795	22.325	-7.747	1.00	20.61
A	C							
ATOM	602	CD2	PHE A 111	15.793	21.381	-6.866	1.00	19.71
A	C							
ATOM	603	CE1	PHE A 111	17.101	23.461	-8.135	1.00	20.07
A	C							
ATOM	604	CE2	PHE A 111	15.085	22.520	-7.254	1.00	20.77
A	C							
ATOM	605	CZ	PHE A 111	15.742	23.557	-7.890	1.00	22.06
A	C							

ATOM	606	C	PHE A 111	19.281	18.070	-7.561	1.00	23.53
A	C							
ATOM	607	O	PHE A 111	19.819	18.082	-6.453	1.00	21.50
A	O							
ATOM	608	N	GLN A 112	19.528	17.125	-8.468	1.00	24.20
A	N							
ATOM	609	CA	GLN A 112	20.486	16.042	-8.215	1.00	24.96
A	C							
ATOM	610	CB	GLN A 112	20.397	14.962	-9.304	1.00	27.91
A	C							
ATOM	611	CG	GLN A 112	19.033	14.309	-9.375	1.00	32.20
A	C							
ATOM	612	CD	GLN A 112	18.866	13.316	-10.503	1.00	36.00
A	C							
ATOM	613	OE1	GLN A 112	17.772	12.806	-10.719	1.00	37.02
A	O							
ATOM	614	NE2	GLN A 112	19.946	13.033	-11.225	1.00	37.13
A	N							
ATOM	615	C	GLN A 112	21.897	16.630	-8.196	1.00	26.21
A	C							
ATOM	616	O	GLN A 112	22.184	17.597	-8.908	1.00	27.42
A	O							
ATOM	617	N	PRO A 113	22.806	16.047	-7.392	1.00	25.53
A	N							
ATOM	618	CD	PRO A 113	24.251	16.272	-7.577	1.00	25.70
A	C							
ATOM	619	CA	PRO A 113	22.577	14.900	-6.506	1.00	25.89
A	C							
ATOM	620	CB	PRO A 113	23.853	14.098	-6.695	1.00	26.16
A	C							
ATOM	621	CG	PRO A 113	24.876	15.203	-6.687	1.00	25.44
A	C							
ATOM	622	C	PRO A 113	22.385	15.287	-5.032	1.00	25.87
A	C							
ATOM	623	O	PRO A 113	22.095	14.434	-4.195	1.00	25.05
A	O							
ATOM	624	N	TYR A 114	22.541	16.571	-4.717	1.00	26.68
A	N							
ATOM	625	CA	TYR A 114	22.430	17.029	-3.331	1.00	27.34
A	C							
ATOM	626	CB	TYR A 114	22.838	18.510	-3.228	1.00	30.74
A	C							
ATOM	627	CG	TYR A 114	24.167	18.813	-3.898	1.00	33.96
A	C							
ATOM	628	CD1	TYR A 114	25.228	17.916	-3.804	1.00	36.01
A	C							
ATOM	629	CE1	TYR A 114	26.435	18.161	-4.438	1.00	38.72
A	C							
ATOM	630	CD2	TYR A 114	24.354	19.979	-4.648	1.00	35.86
A	C							
ATOM	631	CE2	TYR A 114	25.568	20.238	-5.290	1.00	37.49
A	C							
ATOM	632	CZ	TYR A 114	26.601	19.321	-5.178	1.00	39.49
A	C							
ATOM	633	OH	TYR A 114	27.809	19.560	-5.789	1.00	40.81
A	O							
ATOM	634	C	TYR A 114	21.069	16.810	-2.677	1.00	26.15
A	C							

ATOM	635	O	TYR A 114	20.987	16.549	-1.476	1.00	24.90
A	O							
ATOM	636	N	MET A 115	20.006	16.906	-3.467	1.00	25.38
A	N							
ATOM	637	CA	MET A 115	18.662	16.721	-2.948	1.00	24.05
A	C							
ATOM	638	CB	MET A 115	17.646	16.865	-4.084	1.00	24.96
A	C							
ATOM	639	CG	MET A 115	16.206	16.603	-3.708	1.00	24.12
A	C							
ATOM	640	SD	MET A 115	15.563	17.820	-2.574	1.00	23.41
A	S							
ATOM	641	CE	MET A 115	15.122	19.162	-3.708	1.00	23.60
A	C							
ATOM	642	C	MET A 115	18.535	15.348	-2.300	1.00	24.70
A	C							
ATOM	643	O	MET A 115	17.980	15.225	-1.218	1.00	22.93
A	O							
ATOM	644	N	GLN A 116	19.085	14.327	-2.951	1.00	23.45
A	N							
ATOM	645	CA	GLN A 116	19.005	12.962	-2.453	1.00	23.38
A	C							
ATOM	646	CB	GLN A 116	19.439	12.001	-3.561	1.00	25.27
A	C							
ATOM	647	CG	GLN A 116	18.491	12.034	-4.765	1.00	28.21
A	C							
ATOM	648	CD	GLN A 116	18.550	13.344	-5.550	1.00	29.58
A	C							
ATOM	649	OE1	GLN A 116	17.549	13.786	-6.116	1.00	32.33
A	O							
ATOM	650	NE2	GLN A 116	19.727	13.956	-5.600	1.00	27.60
A	N							
ATOM	651	C	GLN A 116	19.766	12.683	-1.160	1.00	21.18
A	C							
ATOM	652	O	GLN A 116	19.570	11.650	-0.527	1.00	21.75
A	O							
ATOM	653	N	GLU A 117	20.632	13.603	-0.761	1.00	19.23
A	N							
ATOM	654	CA	GLU A 117	21.383	13.426	0.472	1.00	18.78
A	C							
ATOM	655	CB	GLU A 117	22.834	13.851	0.272	1.00	22.01
A	C							
ATOM	656	CG	GLU A 117	23.574	13.015	-0.751	1.00	26.21
A	C							
ATOM	657	CD	GLU A 117	25.011	13.446	-0.915	1.00	28.09
A	C							
ATOM	658	OE1	GLU A 117	25.245	14.584	-1.373	1.00	31.04
A	O							
ATOM	659	OE2	GLU A 117	25.907	12.643	-0.583	1.00	29.29
A	O							
ATOM	660	C	GLU A 117	20.765	14.252	1.592	1.00	15.64
A	C							
ATOM	661	O	GLU A 117	20.748	13.834	2.742	1.00	12.05
A	O							
ATOM	662	N	VAL A 118	20.247	15.423	1.233	1.00	12.54
A	N							
ATOM	663	CA	VAL A 118	19.643	16.340	2.190	1.00	10.94
A	C							

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ATOM	664	CB	VAL	A	118	19.521	17.752	1.571	1.00	13.38
A	C									
ATOM	665	CG1	VAL	A	118	18.818	18.689	2.529	1.00	11.25
A	C									
ATOM	666	CG2	VAL	A	118	20.913	18.285	1.227	1.00	11.27
A	C									
ATOM	667	C	VAL	A	118	18.266	15.887	2.686	1.00	12.41
A	C									
ATOM	668	O	VAL	A	118	17.971	15.999	3.872	1.00	12.25
A	O									
ATOM	669	N	VAL	A	119	17.427	15.372	1.793	1.00	11.42
A	N									
ATOM	670	CA	VAL	A	119	16.097	14.942	2.208	1.00	13.06
A	C									
ATOM	671	CB	VAL	A	119	15.275	14.419	1.007	1.00	14.89
A	C									
ATOM	672	CG1	VAL	A	119	14.001	13.738	1.495	1.00	13.96
A	C									
ATOM	673	CG2	VAL	A	119	14.937	15.586	0.072	1.00	12.52
A	C									
ATOM	674	C	VAL	A	119	16.123	13.902	3.337	1.00	12.86
A	C									
ATOM	675	O	VAL	A	119	15.425	14.069	4.335	1.00	13.99
A	O									
ATOM	676	N	PRO	A	120	16.933	12.832	3.208	1.00	13.22
A	N									
ATOM	677	CD	PRO	A	120	17.731	12.385	2.052	1.00	13.49
A	C									
ATOM	678	CA	PRO	A	120	16.979	11.825	4.274	1.00	13.95
A	C									
ATOM	679	CB	PRO	A	120	17.979	10.798	3.743	1.00	13.50
A	C									
ATOM	680	CG	PRO	A	120	17.776	10.882	2.264	1.00	16.77
A	C									
ATOM	681	C	PRO	A	120	17.427	12.439	5.590	1.00	13.93
A	C									
ATOM	682	O	PRO	A	120	16.951	12.058	6.652	1.00	13.50
A	O									
ATOM	683	N	PHE	A	121	18.357	13.385	5.508	1.00	11.40
A	N									
ATOM	684	CA	PHE	A	121	18.860	14.078	6.692	1.00	11.01
A	C									
ATOM	685	CB	PHE	A	121	19.978	15.048	6.270	1.00	10.39
A	C									
ATOM	686	CG	PHE	A	121	20.327	16.085	7.309	1.00	12.29
A	C									
ATOM	687	CD1	PHE	A	121	20.796	15.713	8.561	1.00	10.86
A	C									
ATOM	688	CD2	PHE	A	121	20.220	17.440	7.011	1.00	12.84
A	C									
ATOM	689	CE1	PHE	A	121	21.153	16.678	9.506	1.00	11.52
A	C									
ATOM	690	CE2	PHE	A	121	20.573	18.416	7.951	1.00	13.64
A	C									
ATOM	691	CZ	PHE	A	121	21.042	18.034	9.195	1.00	11.27
A	C									
ATOM	692	C	PHE	A	121	17.715	14.837	7.383	1.00	9.92
A	C									

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ATOM	693	O	PHE A 121	17.474	14.658	8.575	1.00	10.41
A	O							
ATOM	694	N	LEU A 122	17.003	15.673	6.631	1.00	8.04
A	N							
ATOM	695	CA	LEU A 122	15.895	16.445	7.202	1.00	9.54
A	C							
ATOM	696	CB	LEU A 122	15.364	17.439	6.167	1.00	9.32
A	C							
ATOM	697	CG	LEU A 122	16.417	18.482	5.780	1.00	10.24
A	C							
ATOM	698	CD1	LEU A 122	15.888	19.366	4.658	1.00	12.89
A	C							
ATOM	699	CD2	LEU A 122	16.779	19.325	6.997	1.00	10.42
A	C							
ATOM	700	C	LEU A 122	14.765	15.551	7.714	1.00	9.19
A	C							
ATOM	701	O	LEU A 122	14.133	15.853	8.729	1.00	11.17
A	O							
ATOM	702	N	ALA A 123	14.508	14.454	7.012	1.00	10.07
A	N							
ATOM	703	CA	ALA A 123	13.473	13.518	7.432	1.00	11.76
A	C							
ATOM	704	CB	ALA A 123	13.307	12.415	6.385	1.00	11.58
A	C							
ATOM	705	C	ALA A 123	13.844	12.901	8.785	1.00	12.42
A	C							
ATOM	706	O	ALA A 123	12.972	12.651	9.629	1.00	10.87
A	O							
ATOM	707	N	ARG A 124	15.129	12.637	8.996	1.00	13.52
A	N							
ATOM	708	CA	ARG A 124	15.537	12.057	10.268	1.00	15.12
A	C							
ATOM	709	CB	ARG A 124	16.998	11.599	10.230	1.00	16.39
A	C							
ATOM	710	CG	ARG A 124	17.222	10.361	9.361	1.00	18.81
A	C							
ATOM	711	CD	ARG A 124	18.514	9.644	9.730	1.00	19.88
A	C							
ATOM	712	NE	ARG A 124	19.684	10.503	9.592	1.00	21.22
A	N							
ATOM	713	CZ	ARG A 124	20.241	10.818	8.429	1.00	21.14
A	C							
ATOM	714	NH1	ARG A 124	19.739	10.339	7.300	1.00	21.19
A	N							
ATOM	715	NH2	ARG A 124	21.292	11.620	8.398	1.00	21.84
A	N							
ATOM	716	C	ARG A 124	15.319	13.052	11.396	1.00	14.67
A	C							
ATOM	717	O	ARG A 124	14.968	12.666	12.509	1.00	14.02
A	O							
ATOM	718	N	LEU A 125	15.512	14.336	11.113	1.00	12.38
A	N							
ATOM	719	CA	LEU A 125	15.305	15.348	12.142	1.00	12.66
A	C							
ATOM	720	CB	LEU A 125	15.757	16.724	11.655	1.00	11.19
A	C							
ATOM	721	CG	LEU A 125	17.257	16.863	11.400	1.00	12.07
A	C							

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ATOM	722	CD1	LEU	A	125	17.571	18.262	10.880	1.00	11.21
A	C									
ATOM	723	CD2	LEU	A	125	18.015	16.567	12.691	1.00	10.90
A	C									
ATOM	724	C	LEU	A	125	13.824	15.384	12.457	1.00	12.64
A	C									
ATOM	725	O	LEU	A	125	13.424	15.502	13.615	1.00	13.64
A	O									
ATOM	726	N	SER	A	126	13.010	15.289	11.412	1.00	11.87
A	N									
ATOM	727	CA	SER	A	126	11.567	15.301	11.584	1.00	12.10
A	C									
ATOM	728	CB	SER	A	126	10.869	15.199	10.219	1.00	12.32
A	C									
ATOM	729	OG	SER	A	126	9.511	14.794	10.350	1.00	12.93
A	O									
ATOM	730	C	SER	A	126	11.174	14.124	12.466	1.00	14.19
A	C									
ATOM	731	O	SER	A	126	10.379	14.267	13.397	1.00	14.24
A	O									
ATOM	732	N	ASN	A	127	11.751	12.960	12.182	1.00	15.34
A	N									
ATOM	733	CA	ASN	A	127	11.441	11.761	12.953	1.00	19.77
A	C									
ATOM	734	CB	ASN	A	127	12.143	10.532	12.363	1.00	22.15
A	C									
ATOM	735	CG	ASN	A	127	11.687	9.236	13.020	1.00	27.13
A	C									
ATOM	736	OD1	ASN	A	127	10.492	8.925	13.039	1.00	29.33
A	O									
ATOM	737	ND2	ASN	A	127	12.634	8.479	13.564	1.00	27.25
A	N									
ATOM	738	C	ASN	A	127	11.839	11.922	14.416	1.00	19.60
A	C									
ATOM	739	O	ASN	A	127	11.162	11.412	15.305	1.00	19.90
A	O									
ATOM	740	N	ARG	A	128	12.934	12.629	14.672	1.00	19.27
A	N									
ATOM	741	CA	ARG	A	128	13.396	12.855	16.043	1.00	20.04
A	C									
ATOM	742	CB	ARG	A	128	14.783	13.534	15.992	1.00	20.58
A	C									
ATOM	743	CG	ARG	A	128	15.659	13.507	17.262	1.00	24.13
A	C									
ATOM	744	CD	ARG	A	128	15.120	14.392	18.371	1.00	27.44
A	C									
ATOM	745	NE	ARG	A	128	16.165	14.909	19.249	1.00	27.58
A	N									
ATOM	746	CZ	ARG	A	128	15.991	15.179	20.539	1.00	29.81
A	C									
ATOM	747	NH1	ARG	A	128	14.809	14.970	21.107	1.00	29.81
A	N									
ATOM	748	NH2	ARG	A	128	16.991	15.671	21.256	1.00	27.09
A	N									
ATOM	749	C	ARG	A	128	12.373	13.743	16.788	1.00	20.54
A	C									
ATOM	750	O	ARG	A	128	12.069	13.519	17.967	1.00	18.67
A	O									

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ATOM	751	N	LEU	A	129	11.850	14.753	16.098	1.00	19.98
A	N									
ATOM	752	CA	LEU	A	129	10.876	15.669	16.695	1.00	21.90
A	C									
ATOM	753	CB	LEU	A	129	10.813	16.965	15.886	1.00	19.92
A	C									
ATOM	754	CG	LEU	A	129	12.044	17.872	15.908	1.00	19.27
A	C									
ATOM	755	CD1	LEU	A	129	11.925	18.930	14.824	1.00	19.33
A	C									
ATOM	756	CD2	LEU	A	129	12.188	18.504	17.287	1.00	16.10
A	C									
ATOM	757	C	LEU	A	129	9.474	15.075	16.750	1.00	25.34
A	C									
ATOM	758	O	LEU	A	129	8.592	15.579	17.452	1.00	25.92
A	O									
ATOM	759	N	SER	A	130	9.270	14.007	15.994	1.00	28.06
A	N									
ATOM	760	CA	SER	A	130	7.969	13.364	15.910	1.00	33.42
A	C									
ATOM	761	CB	SER	A	130	8.095	11.979	15.288	1.00	32.53
A	C									
ATOM	762	OG	SER	A	130	8.750	11.096	16.177	1.00	35.12
A	O									
ATOM	763	C	SER	A	130	7.200	13.233	17.210	1.00	36.11
A	C									
ATOM	764	O	SER	A	130	7.681	12.658	18.190	1.00	38.33
A	O									
ATOM	765	N	THR	A	131	5.993	13.785	17.200	1.00	39.23
A	N									
ATOM	766	CA	THR	A	131	5.098	13.700	18.340	1.00	42.38
A	C									
ATOM	767	CB	THR	A	131	4.968	12.214	18.733	1.00	44.32
A	C									
ATOM	768	OG1	THR	A	131	4.843	11.445	17.527	1.00	47.57
A	O									
ATOM	769	CG2	THR	A	131	3.725	11.944	19.561	1.00	45.19
A	C									
ATOM	770	C	THR	A	131	5.448	14.576	19.558	1.00	42.64
A	C									
ATOM	771	O	THR	A	131	4.710	14.560	20.551	1.00	43.84
A	O									
ATOM	772	N	CYS	A	132	6.559	15.325	19.496	1.00	41.52
A	N									
ATOM	773	CA	CYS	A	132	6.930	16.219	20.603	1.00	39.84
A	C									
ATOM	774	C	CYS	A	132	5.899	17.299	20.541	1.00	40.10
A	C									
ATOM	775	O	CYS	A	132	5.358	17.570	19.471	1.00	40.22
A	O									
ATOM	776	CB	CYS	A	132	8.309	16.869	20.413	1.00	36.93
A	C									
ATOM	777	SG	CYS	A	132	8.480	18.000	18.999	1.00	32.53
A	S									
ATOM	778	N	HIS	A	133	5.624	17.927	21.673	1.00	40.74
A	N									
ATOM	779	CA	HIS	A	133	4.629	18.979	21.689	1.00	41.87
A	C									

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ATOM	780	CB	HIS	A	133	3.251	18.373	21.933	1.00	44.51
A	C									
ATOM	781	CG	HIS	A	133	3.122	17.694	23.260	1.00	47.49
A	C									
ATOM	782	CD2	HIS	A	133	2.913	16.396	23.583	1.00	48.42
A	C									
ATOM	783	ND1	HIS	A	133	3.241	18.371	24.455	1.00	48.25
A	N									
ATOM	784	CE1	HIS	A	133	3.114	17.518	25.457	1.00	48.41
A	C									
ATOM	785	NE2	HIS	A	133	2.915	16.313	24.955	1.00	48.80
A	N									
ATOM	786	C	HIS	A	133	4.916	20.023	22.750	1.00	41.49
A	C									
ATOM	787	O	HIS	A	133	5.897	19.924	23.488	1.00	40.33
A	O									
ATOM	788	N	ILE	A	134	4.050	21.030	22.811	1.00	41.32
A	N									
ATOM	789	CA	ILE	A	134	4.176	22.099	23.794	1.00	42.67
A	C									
ATOM	790	CB	ILE	A	134	4.176	23.493	23.120	1.00	42.74
A	C									
ATOM	791	CG2	ILE	A	134	5.446	23.663	22.301	1.00	42.04
A	C									
ATOM	792	CG1	ILE	A	134	2.918	23.649	22.255	1.00	41.70
A	C									
ATOM	793	CD	ILE	A	134	2.780	24.957	21.499	1.00	41.81
A	C									
ATOM	794	C	ILE	A	134	3.000	21.999	24.763	1.00	43.64
A	C									
ATOM	795	O	ILE	A	134	1.906	21.571	24.387	1.00	43.52
A	O									
ATOM	796	N	GLU	A	135	3.229	22.391	26.011	1.00	44.33
A	N									
ATOM	797	CA	GLU	A	135	2.189	22.319	27.031	1.00	45.59
A	C									
ATOM	798	CB	GLU	A	135	2.832	22.272	28.431	1.00	47.61
A	C									
ATOM	799	CG	GLU	A	135	3.765	23.448	28.742	1.00	50.52
A	C									
ATOM	800	CD	GLU	A	135	4.589	23.260	30.002	1.00	51.87
A	C									
ATOM	801	OE1	GLU	A	135	5.538	22.454	29.942	1.00	51.72
A	O									
ATOM	802	OE2	GLU	A	135	4.301	23.912	31.037	1.00	52.55
A	O									
ATOM	803	C	GLU	A	135	1.191	23.474	26.938	1.00	45.27
A	C									
ATOM	804	O	GLU	A	135	0.204	23.512	27.674	1.00	45.54
A	O									
ATOM	805	N	GLY	A	136	1.447	24.415	26.033	1.00	44.63
A	N									
ATOM	806	CA	GLY	A	136	0.557	25.553	25.878	1.00	43.02
A	C									
ATOM	807	C	GLY	A	136	-0.268	25.466	24.612	1.00	42.19
A	C									
ATOM	808	O	GLY	A	136	-0.205	24.469	23.894	1.00	42.03
A	O									

ATOM	809	N	ASP	A	137	-1.048	26.507	24.341	1.00	41.98
A	N									
ATOM	810	CA	ASP	A	137	-1.881	26.544	23.146	1.00	41.03
A	C									
ATOM	811	CB	ASP	A	137	-2.996	27.576	23.310	1.00	43.41
A	C									
ATOM	812	CG	ASP	A	137	-3.844	27.710	22.064	1.00	45.06
A	C									
ATOM	813	OD1	ASP	A	137	-4.458	26.704	21.647	1.00	47.37
A	O									
ATOM	814	OD2	ASP	A	137	-3.892	28.821	21.499	1.00	45.71
A	O									
ATOM	815	C	ASP	A	137	-1.016	26.908	21.944	1.00	39.51
A	C									
ATOM	816	O	ASP	A	137	-0.162	27.783	22.036	1.00	39.46
A	O									
ATOM	817	N	ASP	A	138	-1.241	26.244	20.814	1.00	38.39
A	N									
ATOM	818	CA	ASP	A	138	-0.439	26.511	19.621	1.00	37.99
A	C									
ATOM	819	CB	ASP	A	138	0.168	25.208	19.102	1.00	39.01
A	C									
ATOM	820	CG	ASP	A	138	-0.874	24.264	18.548	1.00	39.32
A	C									
ATOM	821	OD1	ASP	A	138	-2.070	24.475	18.826	1.00	39.65
A	O									
ATOM	822	OD2	ASP	A	138	-0.500	23.307	17.842	1.00	41.75
A	O									
ATOM	823	C	ASP	A	138	-1.219	27.186	18.501	1.00	36.81
A	C									
ATOM	824	O	ASP	A	138	-0.832	27.116	17.335	1.00	35.87
A	O									
ATOM	825	N	LEU	A	139	-2.315	27.849	18.857	1.00	34.57
A	N									
ATOM	826	CA	LEU	A	139	-3.139	28.532	17.870	1.00	33.64
A	C									
ATOM	827	CB	LEU	A	139	-4.321	29.219	18.563	1.00	34.78
A	C									
ATOM	828	CG	LEU	A	139	-5.618	29.352	17.757	1.00	36.95
A	C									
ATOM	829	CD1	LEU	A	139	-6.663	30.071	18.602	1.00	36.17
A	C									
ATOM	830	CD2	LEU	A	139	-5.364	30.112	16.464	1.00	36.43
A	C									
ATOM	831	C	LEU	A	139	-2.326	29.561	17.079	1.00	31.14
A	C									
ATOM	832	O	LEU	A	139	-2.461	29.666	15.862	1.00	30.79
A	O									
ATOM	833	N	HIS	A	140	-1.483	30.318	17.769	1.00	29.61
A	N									
ATOM	834	CA	HIS	A	140	-0.671	31.329	17.103	1.00	29.77
A	C									
ATOM	835	CB	HIS	A	140	0.039	32.210	18.138	1.00	32.63
A	C									
ATOM	836	CG	HIS	A	140	0.926	31.453	19.078	1.00	35.82
A	C									
ATOM	837	CD2	HIS	A	140	2.183	31.706	19.515	1.00	36.65
A	C									

ATOM	838	ND1	HIS	A	140	0.524	30.297	19.713	1.00	37.28
A	N									
ATOM	839	CE1	HIS	A	140	1.496	29.870	20.500	1.00	38.18
A	C									
ATOM	840	NE2	HIS	A	140	2.514	30.707	20.399	1.00	36.65
A	N									
ATOM	841	C	HIS	A	140	0.342	30.664	16.180	1.00	28.45
A	C									
ATOM	842	O	HIS	A	140	0.639	31.171	15.102	1.00	28.05
A	O									
ATOM	843	N	ILE	A	141	0.857	29.514	16.597	1.00	27.82
A	N									
ATOM	844	CA	ILE	A	141	1.825	28.784	15.790	1.00	26.79
A	C									
ATOM	845	CB	ILE	A	141	2.424	27.616	16.595	1.00	26.52
A	C									
ATOM	846	CG2	ILE	A	141	3.057	26.598	15.667	1.00	24.81
A	C									
ATOM	847	CG1	ILE	A	141	3.434	28.174	17.605	1.00	26.50
A	C									
ATOM	848	CD	ILE	A	141	3.981	27.146	18.563	1.00	28.45
A	C									
ATOM	849	C	ILE	A	141	1.168	28.269	14.516	1.00	27.29
A	C									
ATOM	850	O	ILE	A	141	1.749	28.344	13.434	1.00	26.99
A	O									
ATOM	851	N	GLN	A	142	-0.053	27.760	14.647	1.00	28.53
A	N									
ATOM	852	CA	GLN	A	142	-0.788	27.249	13.497	1.00	27.65
A	C									
ATOM	853	CB	GLN	A	142	-2.128	26.667	13.940	1.00	29.20
A	C									
ATOM	854	CG	GLN	A	142	-2.026	25.340	14.674	1.00	32.99
A	C									
ATOM	855	CD	GLN	A	142	-3.388	24.786	15.049	1.00	35.51
A	C									
ATOM	856	OE1	GLN	A	142	-4.111	25.378	15.850	1.00	40.18
A	O									
ATOM	857	NE2	GLN	A	142	-3.748	23.651	14.464	1.00	36.87
A	N									
ATOM	858	C	GLN	A	142	-1.025	28.354	12.473	1.00	26.74
A	C									
ATOM	859	O	GLN	A	142	-0.895	28.132	11.272	1.00	26.24
A	O									
ATOM	860	N	ARG	A	143	-1.376	29.542	12.953	1.00	27.29
A	N									
ATOM	861	CA	ARG	A	143	-1.622	30.679	12.071	1.00	27.82
A	C									
ATOM	862	CB	ARG	A	143	-2.106	31.886	12.878	1.00	29.63
A	C									
ATOM	863	CG	ARG	A	143	-3.526	31.758	13.405	1.00	34.47
A	C									
ATOM	864	CD	ARG	A	143	-3.788	32.781	14.507	1.00	39.86
A	C									
ATOM	865	NE	ARG	A	143	-5.170	32.741	14.977	1.00	44.13
A	N									
ATOM	866	CZ	ARG	A	143	-5.575	33.213	16.152	1.00	46.89
A	C									

ATOM	867	NH1	ARG	A	143	-4.701	33.762	16.987	1.00	47.65
A	N									
ATOM	868	NH2	ARG	A	143	-6.856	33.132	16.493	1.00	48.27
A	N									
ATOM	869	C	ARG	A	143	-0.363	31.064	11.301	1.00	26.24
A	C									
ATOM	870	O	ARG	A	143	-0.410	31.289	10.094	1.00	24.10
A	O									
ATOM	871	N	ASN	A	144	0.761	31.136	12.004	1.00	25.57
A	N									
ATOM	872	CA	ASN	A	144	2.024	31.511	11.377	1.00	25.34
A	C									
ATOM	873	CB	ASN	A	144	3.113	31.670	12.442	1.00	25.23
A	C									
ATOM	874	CG	ASN	A	144	2.901	32.901	13.310	1.00	27.47
A	C									
ATOM	875	OD1	ASN	A	144	1.855	33.552	13.238	1.00	25.19
A	O									
ATOM	876	ND2	ASN	A	144	3.894	33.225	14.137	1.00	26.15
A	N									
ATOM	877	C	ASN	A	144	2.460	30.508	10.319	1.00	24.78
A	C									
ATOM	878	O	ASN	A	144	2.963	30.896	9.259	1.00	24.90
A	O									
ATOM	879	N	VAL	A	145	2.262	29.222	10.599	1.00	23.95
A	N									
ATOM	880	CA	VAL	A	145	2.638	28.177	9.650	1.00	22.12
A	C									
ATOM	881	CB	VAL	A	145	2.578	26.771	10.298	1.00	22.24
A	C									
ATOM	882	CG1	VAL	A	145	2.893	25.703	9.265	1.00	22.51
A	C									
ATOM	883	CG2	VAL	A	145	3.571	26.688	11.442	1.00	19.36
A	C									
ATOM	884	C	VAL	A	145	1.705	28.219	8.445	1.00	23.02
A	C									
ATOM	885	O	VAL	A	145	2.143	28.075	7.304	1.00	20.64
A	O									
ATOM	886	N	GLN	A	146	0.417	28.430	8.703	1.00	24.15
A	N									
ATOM	887	CA	GLN	A	146	-0.566	28.491	7.630	1.00	23.03
A	C									
ATOM	888	CB	GLN	A	146	-1.962	28.746	8.197	1.00	25.85
A	C									
ATOM	889	CG	GLN	A	146	-3.056	28.631	7.153	1.00	27.55
A	C									
ATOM	890	CD	GLN	A	146	-3.028	27.291	6.443	1.00	27.72
A	C									
ATOM	891	OE1	GLN	A	146	-2.920	27.228	5.221	1.00	28.53
A	O									
ATOM	892	NE2	GLN	A	146	-3.125	26.210	7.210	1.00	29.98
A	N									
ATOM	893	C	GLN	A	146	-0.227	29.586	6.625	1.00	23.12
A	C									
ATOM	894	O	GLN	A	146	-0.409	29.411	5.422	1.00	22.07
A	O									
ATOM	895	N	LYS	A	147	0.253	30.720	7.120	1.00	21.60
A	N									

ATOM	896	CA	LYS A 147	0.609	31.826	6.242	1.00	23.99
A	C							
ATOM	897	CB	LYS A 147	0.982	33.069	7.054	1.00	27.26
A	C							
ATOM	898	CG	LYS A 147	1.356	34.266	6.183	1.00	33.40
A	C							
ATOM	899	CD	LYS A 147	0.223	34.614	5.211	1.00	37.04
A	C							
ATOM	900	CE	LYS A 147	0.599	35.760	4.278	1.00	38.65
A	C							
ATOM	901	NZ	LYS A 147	0.882	37.019	5.027	1.00	40.65
A	N							
ATOM	902	C	LYS A 147	1.778	31.441	5.349	1.00	24.34
A	C							
ATOM	903	O	LYS A 147	1.860	31.861	4.193	1.00	21.81
A	O							
ATOM	904	N	LEU A 148	2.696	30.650	5.894	1.00	23.83
A	N							
ATOM	905	CA	LEU A 148	3.844	30.216	5.120	1.00	23.73
A	C							
ATOM	906	CB	LEU A 148	4.864	29.516	6.029	1.00	24.60
A	C							
ATOM	907	CG	LEU A 148	6.213	29.108	5.425	1.00	25.23
A	C							
ATOM	908	CD1	LEU A 148	7.213	28.802	6.539	1.00	27.40
A	C							
ATOM	909	CD2	LEU A 148	6.023	27.897	4.535	1.00	25.60
A	C							
ATOM	910	C	LEU A 148	3.315	29.272	4.043	1.00	21.03
A	C							
ATOM	911	O	LEU A 148	3.706	29.364	2.885	1.00	22.18
A	O							
ATOM	912	N	LYS A 149	2.411	28.376	4.422	1.00	21.82
A	N							
ATOM	913	CA	LYS A 149	1.834	27.439	3.461	1.00	22.95
A	C							
ATOM	914	CB	LYS A 149	0.852	26.495	4.148	1.00	24.40
A	C							
ATOM	915	CG	LYS A 149	1.462	25.605	5.209	1.00	26.03
A	C							
ATOM	916	CD	LYS A 149	0.433	24.591	5.683	1.00	29.36
A	C							
ATOM	917	CE	LYS A 149	1.026	23.603	6.667	1.00	31.50
A	C							
ATOM	918	NZ	LYS A 149	0.039	22.535	7.000	1.00	33.82
A	N							
ATOM	919	C	LYS A 149	1.098	28.204	2.366	1.00	23.21
A	C							
ATOM	920	O	LYS A 149	1.239	27.899	1.177	1.00	21.94
A	O							
ATOM	921	N	ASP A 150	0.319	29.203	2.771	1.00	22.28
A	N							
ATOM	922	CA	ASP A 150	-0.441	30.003	1.814	1.00	23.20
A	C							
ATOM	923	CB	ASP A 150	-1.303	31.054	2.526	1.00	25.06
A	C							
ATOM	924	CG	ASP A 150	-2.359	30.444	3.430	1.00	27.96
A	C							

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ATOM	925	OD1	ASP	A	150	-2.832	29.327	3.140	1.00	29.25
A	O									
ATOM	926	OD2	ASP	A	150	-2.731	31.100	4.428	1.00	30.84
A	O									
ATOM	927	C	ASP	A	150	0.487	30.716	0.844	1.00	22.09
A	C									
ATOM	928	O	ASP	A	150	0.201	30.804	-0.349	1.00	22.07
A	O									
ATOM	929	N	THR	A	151	1.599	31.228	1.360	1.00	20.13
A	N									
ATOM	930	CA	THR	A	151	2.557	31.949	0.533	1.00	20.21
A	C									
ATOM	931	CB	THR	A	151	3.676	32.578	1.390	1.00	21.32
A	C									
ATOM	932	OG1	THR	A	151	3.097	33.422	2.392	1.00	22.82
A	O									
ATOM	933	CG2	THR	A	151	4.602	33.410	0.520	1.00	23.30
A	C									
ATOM	934	C	THR	A	151	3.184	31.045	-0.521	1.00	19.34
A	C									
ATOM	935	O	THR	A	151	3.403	31.466	-1.659	1.00	16.62
A	O									
ATOM	936	N	VAL	A	152	3.482	29.809	-0.134	1.00	17.83
A	N									
ATOM	937	CA	VAL	A	152	4.071	28.849	-1.056	1.00	20.82
A	C									
ATOM	938	CB	VAL	A	152	4.465	27.545	-0.322	1.00	19.02
A	C									
ATOM	939	CG1	VAL	A	152	4.739	26.433	-1.323	1.00	21.92
A	C									
ATOM	940	CG2	VAL	A	152	5.716	27.782	0.507	1.00	20.80
A	C									
ATOM	941	C	VAL	A	152	3.087	28.535	-2.183	1.00	22.16
A	C									
ATOM	942	O	VAL	A	152	3.479	28.449	-3.346	1.00	23.43
A	O									
ATOM	943	N	LYS	A	153	1.810	28.379	-1.843	1.00	24.38
A	N									
ATOM	944	CA	LYS	A	153	0.789	28.087	-2.849	1.00	27.82
A	C									
ATOM	945	CB	LYS	A	153	-0.534	27.732	-2.176	1.00	31.58
A	C									
ATOM	946	CG	LYS	A	153	-0.441	26.583	-1.209	1.00	35.04
A	C									
ATOM	947	CD	LYS	A	153	-1.778	26.401	-0.548	1.00	40.47
A	C									
ATOM	948	CE	LYS	A	153	-1.689	25.379	0.560	1.00	43.02
A	C									
ATOM	949	NZ	LYS	A	153	-2.952	25.190	1.344	1.00	44.36
A	N									
ATOM	950	C	LYS	A	153	0.585	29.279	-3.784	1.00	29.16
A	C									
ATOM	951	O	LYS	A	153	0.437	29.108	-4.996	1.00	28.68
A	O									
ATOM	952	N	LYS	A	154	0.580	30.484	-3.218	1.00	28.50
A	N									
ATOM	953	CA	LYS	A	154	0.402	31.699	-4.005	1.00	29.69
A	C									

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ATOM	954	CB	LYS A 154	0.479	32.942	-3.106	1.00	32.52
A	C							
ATOM	955	CG	LYS A 154	-0.616	33.048	-2.053	1.00	37.41
A	C							
ATOM	956	CD	LYS A 154	-0.339	34.206	-1.095	1.00	40.74
A	C							
ATOM	957	CE	LYS A 154	-1.385	34.290	0.009	1.00	42.32
A	C							
ATOM	958	NZ	LYS A 154	-1.038	35.319	1.032	1.00	42.89
A	N							
ATOM	959	C	LYS A 154	1.496	31.788	-5.064	1.00	28.78
A	C							
ATOM	960	O	LYS A 154	1.291	32.351	-6.144	1.00	28.74
A	O							
ATOM	961	N	LEU A 155	2.661	31.232	-4.738	1.00	26.21
A	N							
ATOM	962	CA	LEU A 155	3.805	31.253	-5.640	1.00	24.24
A	C							
ATOM	963	CB	LEU A 155	5.118	31.313	-4.847	1.00	22.63
A	C							
ATOM	964	CG	LEU A 155	5.392	32.561	-3.979	1.00	24.03
A	C							
ATOM	965	CD1	LEU A 155	6.695	32.374	-3.263	1.00	25.32
A	C							
ATOM	966	CD2	LEU A 155	5.518	33.828	-4.793	1.00	23.74
A	C							
ATOM	967	C	LEU A 155	3.807	30.058	-6.576	1.00	22.47
A	C							
ATOM	968	O	LEU A 155	4.504	30.059	-7.590	1.00	22.33
A	O							
ATOM	969	N	GLY A 156	3.009	29.051	-6.240	1.00	23.16
A	N							
ATOM	970	CA	GLY A 156	2.927	27.864	-7.068	1.00	22.02
A	C							
ATOM	971	C	GLY A 156	4.208	27.063	-7.063	1.00	21.25
A	C							
ATOM	972	O	GLY A 156	4.829	26.876	-6.020	1.00	21.24
A	O							
ATOM	973	N	GLU A 157	4.604	26.585	-8.236	1.00	20.06
A	N							
ATOM	974	CA	GLU A 157	5.816	25.788	-8.371	1.00	21.41
A	C							
ATOM	975	CB	GLU A 157	6.055	25.449	-9.849	1.00	23.31
A	C							
ATOM	976	CG	GLU A 157	7.319	24.650	-10.107	1.00	28.64
A	C							
ATOM	977	CD	GLU A 157	7.147	23.189	-9.770	1.00	31.67
A	C							
ATOM	978	OE1	GLU A 157	6.397	22.891	-8.824	1.00	34.33
A	O							
ATOM	979	OE2	GLU A 157	7.765	22.334	-10.439	1.00	33.96
A	O							
ATOM	980	C	GLU A 157	7.029	26.539	-7.817	1.00	19.72
A	C							
ATOM	981	O	GLU A 157	7.860	25.971	-7.105	1.00	19.07
A	O							
ATOM	982	N	SER A 158	7.129	27.821	-8.147	1.00	18.69
A	N							

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ATOM	983	CA	SER A 158	8.249	28.624	-7.680	1.00	19.07
A	C							
ATOM	984	CB	SER A 158	8.218	30.006	-8.337	1.00	20.27
A	C							
ATOM	985	OG	SER A 158	7.058	30.717	-7.957	1.00	24.37
A	O							
ATOM	986	C	SER A 158	8.225	28.761	-6.158	1.00	17.90
A	C							
ATOM	987	O	SER A 158	9.214	29.166	-5.549	1.00	16.77
A	O							
ATOM	988	N	GLY A 159	7.088	28.433	-5.552	1.00	15.07
A	N							
ATOM	989	CA	GLY A 159	6.975	28.500	-4.108	1.00	13.85
A	C							
ATOM	990	C	GLY A 159	7.806	27.375	-3.524	1.00	12.96
A	C							
ATOM	991	O	GLY A 159	8.496	27.545	-2.521	1.00	11.66
A	O							
ATOM	992	N	GLU A 160	7.729	26.215	-4.163	1.00	13.13
A	N							
ATOM	993	CA	GLU A 160	8.486	25.046	-3.741	1.00	14.60
A	C							
ATOM	994	CB	GLU A 160	8.017	23.820	-4.522	1.00	16.03
A	C							
ATOM	995	CG	GLU A 160	6.665	23.291	-4.073	1.00	17.68
A	C							
ATOM	996	CD	GLU A 160	6.076	22.326	-5.082	1.00	19.55
A	C							
ATOM	997	OE1	GLU A 160	6.849	21.556	-5.687	1.00	19.93
A	O							
ATOM	998	OE2	GLU A 160	4.843	22.341	-5.266	1.00	24.36
A	O							
ATOM	999	C	GLU A 160	9.972	25.293	-3.988	1.00	13.84
A	C							
ATOM	1000	O	GLU A 160	10.819	24.908	-3.180	1.00	13.51
A	O							
ATOM	1001	N	ILE A 161	10.278	25.941	-5.109	1.00	13.97
A	N							
ATOM	1002	CA	ILE A 161	11.659	26.262	-5.457	1.00	15.01
A	C							
ATOM	1003	CB	ILE A 161	11.752	26.949	-6.853	1.00	16.72
A	C							
ATOM	1004	CG2	ILE A 161	13.191	27.359	-7.146	1.00	15.56
A	C							
ATOM	1005	CG1	ILE A 161	11.225	26.012	-7.947	1.00	16.62
A	C							
ATOM	1006	CD	ILE A 161	11.853	24.641	-7.954	1.00	19.54
A	C							
ATOM	1007	C	ILE A 161	12.220	27.219	-4.399	1.00	14.73
A	C							
ATOM	1008	O	ILE A 161	13.351	27.053	-3.927	1.00	15.29
A	O							
ATOM	1009	N	LYS A 162	11.424	28.216	-4.024	1.00	11.62
A	N							
ATOM	1010	CA	LYS A 162	11.852	29.185	-3.021	1.00	12.12
A	C							
ATOM	1011	CB	LYS A 162	10.787	30.269	-2.829	1.00	12.70
A	C							

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ATOM	1012	CG	LYS A 162	11.098	31.245	-1.697	1.00	11.50
A	C							
ATOM	1013	CD	LYS A 162	10.128	32.416	-1.676	1.00	15.16
A	C							
ATOM	1014	CE	LYS A 162	10.361	33.352	-2.853	1.00	15.54
A	C							
ATOM	1015	NZ	LYS A 162	11.753	33.881	-2.894	1.00	17.14
A	N							
ATOM	1016	C	LYS A 162	12.146	28.503	-1.686	1.00	13.23
A	C							
ATOM	1017	O	LYS A 162	13.160	28.792	-1.050	1.00	13.30
A	O							
ATOM	1018	N	ALA A 163	11.260	27.603	-1.266	1.00	12.38
A	N							
ATOM	1019	CA	ALA A 163	11.438	26.880	-0.009	1.00	12.47
A	C							
ATOM	1020	CB	ALA A 163	10.286	25.913	0.211	1.00	12.98
A	C							
ATOM	1021	C	ALA A 163	12.756	26.117	-0.011	1.00	13.14
A	C							
ATOM	1022	O	ALA A 163	13.452	26.062	1.008	1.00	12.48
A	O							
ATOM	1023	N	ILE A 164	13.095	25.516	-1.149	1.00	12.42
A	N							
ATOM	1024	CA	ILE A 164	14.346	24.780	-1.260	1.00	11.86
A	C							
ATOM	1025	CB	ILE A 164	14.435	23.993	-2.589	1.00	12.07
A	C							
ATOM	1026	CG2	ILE A 164	15.731	23.202	-2.635	1.00	10.78
A	C							
ATOM	1027	CG1	ILE A 164	13.262	23.017	-2.718	1.00	12.17
A	C							
ATOM	1028	CD	ILE A 164	13.278	22.229	-4.022	1.00	12.86
A	C							
ATOM	1029	C	ILE A 164	15.491	25.800	-1.204	1.00	12.22
A	C							
ATOM	1030	O	ILE A 164	16.541	25.545	-0.610	1.00	11.10
A	O							
ATOM	1031	N	GLY A 165	15.281	26.955	-1.826	1.00	10.67
A	N							
ATOM	1032	CA	GLY A 165	16.303	27.989	-1.813	1.00	12.02
A	C							
ATOM	1033	C	GLY A 165	16.550	28.534	-0.417	1.00	13.62
A	C							
ATOM	1034	O	GLY A 165	17.609	29.107	-0.140	1.00	12.29
A	O							
ATOM	1035	N	GLU A 166	15.571	28.365	0.468	1.00	12.40
A	N							
ATOM	1036	CA	GLU A 166	15.698	28.837	1.846	1.00	13.51
A	C							
ATOM	1037	CB	GLU A 166	14.395	29.508	2.309	1.00	13.61
A	C							
ATOM	1038	CG	GLU A 166	14.217	30.919	1.757	1.00	16.87
A	C							
ATOM	1039	CD	GLU A 166	13.013	31.651	2.334	1.00	18.65
A	C							
ATOM	1040	OE1	GLU A 166	12.660	31.392	3.504	1.00	15.68
A	O							

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ATOM	1041	OE2	GLU	A	166	12.435	32.507	1.618	1.00	18.26
A	O									
ATOM	1042	C	GLU	A	166	16.068	27.720	2.821	1.00	13.52
A	C									
ATOM	1043	O	GLU	A	166	15.908	27.877	4.028	1.00	12.78
A	O									
ATOM	1044	N	LEU	A	167	16.563	26.594	2.310	1.00	12.05
A	N									
ATOM	1045	CA	LEU	A	167	16.937	25.505	3.203	1.00	11.58
A	C									
ATOM	1046	CB	LEU	A	167	17.366	24.264	2.417	1.00	13.77
A	C									
ATOM	1047	CG	LEU	A	167	16.223	23.441	1.818	1.00	14.22
A	C									
ATOM	1048	CD1	LEU	A	167	16.778	22.130	1.246	1.00	16.24
A	C									
ATOM	1049	CD2	LEU	A	167	15.179	23.155	2.895	1.00	16.98
A	C									
ATOM	1050	C	LEU	A	167	18.048	25.922	4.158	1.00	12.19
A	C									
ATOM	1051	O	LEU	A	167	18.206	25.334	5.233	1.00	11.69
A	O									
ATOM	1052	N	ASP	A	168	18.816	26.937	3.770	1.00	12.76
A	N									
ATOM	1053	CA	ASP	A	168	19.887	27.419	4.625	1.00	13.15
A	C									
ATOM	1054	CB	ASP	A	168	20.843	28.342	3.848	1.00	16.25
A	C									
ATOM	1055	CG	ASP	A	168	20.139	29.497	3.160	1.00	19.91
A	C									
ATOM	1056	OD1	ASP	A	168	18.915	29.421	2.926	1.00	18.66
A	O									
ATOM	1057	OD2	ASP	A	168	20.827	30.487	2.832	1.00	20.94
A	O									
ATOM	1058	C	ASP	A	168	19.279	28.116	5.836	1.00	13.72
A	C									
ATOM	1059	O	ASP	A	168	19.777	27.975	6.953	1.00	15.78
A	O									
ATOM	1060	N	LEU	A	169	18.190	28.851	5.622	1.00	13.06
A	N									
ATOM	1061	CA	LEU	A	169	17.499	29.523	6.717	1.00	13.54
A	C									
ATOM	1062	CB	LEU	A	169	16.525	30.577	6.173	1.00	14.93
A	C									
ATOM	1063	CG	LEU	A	169	17.254	31.653	5.365	1.00	16.86
A	C									
ATOM	1064	CD1	LEU	A	169	16.306	32.688	4.873	1.00	17.37
A	C									
ATOM	1065	CD2	LEU	A	169	18.260	32.337	6.229	1.00	19.91
A	C									
ATOM	1066	C	LEU	A	169	16.738	28.499	7.556	1.00	12.68
A	C									
ATOM	1067	O	LEU	A	169	16.595	28.659	8.770	1.00	13.63
A	O									
ATOM	1068	N	LEU	A	170	16.251	27.446	6.905	1.00	12.87
A	N									
ATOM	1069	CA	LEU	A	170	15.526	26.397	7.604	1.00	12.73
A	C									

ATOM	1070	CB	LEU A 170	14.937	25.387	6.612	1.00	13.33
A	C							
ATOM	1071	CG	LEU A 170	14.185	24.231	7.280	1.00	14.18
A	C							
ATOM	1072	CD1	LEU A 170	13.048	24.789	8.111	1.00	15.94
A	C							
ATOM	1073	CD2	LEU A 170	13.649	23.275	6.225	1.00	15.77
A	C							
ATOM	1074	C	LEU A 170	16.514	25.677	8.506	1.00	11.78
A	C							
ATOM	1075	O	LEU A 170	16.230	25.398	9.671	1.00	10.15
A	O							
ATOM	1076	N	PHE A 171	17.676	25.371	7.947	1.00	12.13
A	N							
ATOM	1077	CA	PHE A 171	18.716	24.684	8.690	1.00	11.64
A	C							
ATOM	1078	CB	PHE A 171	19.938	24.478	7.787	1.00	12.34
A	C							
ATOM	1079	CG	PHE A 171	21.100	23.800	8.465	1.00	13.38
A	C							
ATOM	1080	CD1	PHE A 171	21.980	24.529	9.262	1.00	12.95
A	C							
ATOM	1081	CD2	PHE A 171	21.330	22.438	8.282	1.00	12.74
A	C							
ATOM	1082	CE1	PHE A 171	23.077	23.911	9.862	1.00	12.19
A	C							
ATOM	1083	CE2	PHE A 171	22.426	21.808	8.878	1.00	13.42
A	C							
ATOM	1084	CZ	PHE A 171	23.303	22.549	9.670	1.00	9.66
A	C							
ATOM	1085	C	PHE A 171	19.097	25.487	9.933	1.00	12.85
A	C							
ATOM	1086	O	PHE A 171	19.112	24.956	11.047	1.00	13.16
A	O							
ATOM	1087	N	MET A 172	19.367	26.773	9.739	1.00	12.41
A	N							
ATOM	1088	CA	MET A 172	19.770	27.633	10.845	1.00	13.98
A	C							
ATOM	1089	CB	AMET A 172	20.339	28.952	10.310	0.80	15.64
A	C							
ATOM	1090	CB	BMET A 172	20.370	28.959	10.355	0.20	14.94
A	C							
ATOM	1091	CG	AMET A 172	21.571	28.732	9.435	0.80	16.09
A	C							
ATOM	1092	CG	BMET A 172	19.527	29.804	9.448	0.20	15.64
A	C							
ATOM	1093	SD	AMET A 172	22.552	30.211	9.177	0.80	21.52
A	S							
ATOM	1094	SD	BMET A 172	20.472	31.295	9.068	0.20	14.45
A	S							
ATOM	1095	CE	AMET A 172	21.697	30.932	7.776	0.80	17.67
A	C							
ATOM	1096	CE	BMET A 172	21.541	30.699	7.752	0.20	18.36
A	C							
ATOM	1097	C	MET A 172	18.662	27.902	11.848	1.00	13.07
A	C							
ATOM	1098	O	MET A 172	18.937	28.048	13.039	1.00	13.04
A	O							

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ATOM	1099	N	SER A 173	17.418	27.947	11.379	1.00	13.08
A	N							
ATOM	1100	CA	SER A 173	16.284	28.199	12.261	1.00	11.55
A	C							
ATOM	1101	CB	SER A 173	15.044	28.557	11.440	1.00	11.95
A	C							
ATOM	1102	OG	SER A 173	15.174	29.828	10.818	1.00	14.62
A	O							
ATOM	1103	C	SER A 173	16.019	26.963	13.127	1.00	11.91
A	C							
ATOM	1104	O	SER A 173	15.713	27.082	14.315	1.00	14.96
A	O							
ATOM	1105	N	LEU A 174	16.121	25.777	12.529	1.00	11.90
A	N							
ATOM	1106	CA	LEU A 174	15.927	24.539	13.279	1.00	12.23
A	C							
ATOM	1107	CB	LEU A 174	16.053	23.319	12.351	1.00	13.54
A	C							
ATOM	1108	CG	LEU A 174	14.780	22.851	11.634	1.00	15.89
A	C							
ATOM	1109	CD1	LEU A 174	15.132	21.898	10.491	1.00	14.93
A	C							
ATOM	1110	CD2	LEU A 174	13.845	22.183	12.637	1.00	12.22
A	C							
ATOM	1111	C	LEU A 174	16.999	24.465	14.371	1.00	12.75
A	C							
ATOM	1112	O	LEU A 174	16.710	24.160	15.521	1.00	13.46
A	O							
ATOM	1113	N	ARG A 175	18.243	24.746	13.993	1.00	11.68
A	N							
ATOM	1114	CA	ARG A 175	19.360	24.709	14.930	1.00	14.76
A	C							
ATOM	1115	CB	ARG A 175	20.673	24.990	14.177	1.00	12.95
A	C							
ATOM	1116	CG	ARG A 175	21.888	25.301	15.040	1.00	15.09
A	C							
ATOM	1117	CD	ARG A 175	23.156	25.325	14.175	1.00	13.01
A	C							
ATOM	1118	NE	ARG A 175	24.292	25.954	14.847	1.00	16.67
A	N							
ATOM	1119	CZ	ARG A 175	25.566	25.771	14.505	1.00	15.77
A	C							
ATOM	1120	NH1	ARG A 175	25.888	24.962	13.502	1.00	11.71
A	N							
ATOM	1121	NH2	ARG A 175	26.525	26.429	15.144	1.00	16.45
A	N							
ATOM	1122	C	ARG A 175	19.146	25.733	16.051	1.00	14.85
A	C							
ATOM	1123	O	ARG A 175	19.163	25.392	17.235	1.00	16.14
A	O							
ATOM	1124	N	ASN A 176	18.898	26.978	15.678	1.00	12.31
A	N							
ATOM	1125	CA	ASN A 176	18.708	28.021	16.678	1.00	13.85
A	C							
ATOM	1126	CB	ASN A 176	18.582	29.387	16.000	1.00	11.88
A	C							
ATOM	1127	CG	ASN A 176	19.870	29.825	15.332	1.00	15.20
A	C							

ATOM	1128	OD1	ASN	A	176	20.956	29.382	15.705	1.00	14.68
A	O									
ATOM	1129	ND2	ASN	A	176	19.759	30.709	14.350	1.00	13.94
A	N									
ATOM	1130	C	ASN	A	176	17.519	27.799	17.612	1.00	13.45
A	C									
ATOM	1131	O	ASN	A	176	17.609	28.060	18.812	1.00	13.27
A	O									
ATOM	1132	N	ALA	A	177	16.410	27.303	17.079	1.00	12.70
A	N									
ATOM	1133	CA	ALA	A	177	15.233	27.092	17.913	1.00	13.82
A	C									
ATOM	1134	CB	ALA	A	177	13.961	27.151	17.049	1.00	12.99
A	C									
ATOM	1135	C	ALA	A	177	15.240	25.793	18.701	1.00	13.69
A	C									
ATOM	1136	O	ALA	A	177	14.581	25.693	19.735	1.00	13.56
A	O									
ATOM	1137	N	CYS	A	178	16.013	24.808	18.255	1.00	12.34
A	N									
ATOM	1138	CA	CYS	A	178	15.954	23.505	18.917	1.00	12.68
A	C									
ATOM	1139	C	CYS	A	178	17.144	23.035	19.788	1.00	12.67
A	C									
ATOM	1140	O	CYS	A	178	16.965	22.126	20.591	1.00	12.42
A	O									
ATOM	1141	CB	CYS	A	178	15.703	22.419	17.872	1.00	12.70
A	C									
ATOM	1142	SG	CYS	A	178	14.143	22.611	16.953	1.00	13.36
A	S									
ATOM	1143	N	ILE	A	179	18.323	23.620	19.637	1.00	15.23
A	N									
ATOM	1144	CA	ILE	A	179	19.456	23.173	20.438	1.00	18.51
A	C									
ATOM	1145	CB	ILE	A	179	20.789	23.611	19.808	1.00	17.80
A	C									
ATOM	1146	CG2	ILE	A	179	20.887	23.039	18.390	1.00	15.56
A	C									
ATOM	1147	CG1	ILE	A	179	20.891	25.138	19.793	1.00	17.43
A	C									
ATOM	1148	CD	ILE	A	179	22.185	25.660	19.200	1.00	18.12
A	C									
ATOM	1149	C	ILE	A	179	19.384	23.657	21.886	1.00	22.43
A	C									
ATOM	1150	OT1	ILE	A	179	19.937	22.965	22.766	1.00	24.68
A	O									
ATOM	1151	OT2	ILE	A	179	18.783	24.728	22.123	1.00	25.46
A	O									
ATOM	1152	CB	HIS	B	39	27.892	44.470	-6.060	1.00	45.22
B	C									
ATOM	1153	CG	HIS	B	39	28.041	43.710	-7.341	1.00	48.50
B	C									
ATOM	1154	CD2	HIS	B	39	27.587	42.488	-7.704	1.00	50.10
B	C									
ATOM	1155	ND1	HIS	B	39	28.700	44.216	-8.442	1.00	50.41
B	N									
ATOM	1156	CE1	HIS	B	39	28.644	43.338	-9.428	1.00	50.37
B	C									

ATOM	1157	NE2	HIS	B	39	27.974	42.281	-9.007	1.00	50.98
B	N									
ATOM	1158	C	HIS	B	39	29.987	43.757	-4.873	1.00	43.85
B	C									
ATOM	1159	O	HIS	B	39	31.015	43.319	-5.402	1.00	43.28
B	O									
ATOM	1160	N	HIS	B	39	29.995	45.653	-6.496	1.00	43.51
B	N									
ATOM	1161	CA	HIS	B	39	29.215	44.936	-5.463	1.00	44.10
B	C									
ATOM	1162	N	CYS	B	40	29.484	43.231	-3.770	1.00	42.96
B	N									
ATOM	1163	CA	CYS	B	40	30.174	42.138	-3.125	1.00	42.42
B	C									
ATOM	1164	C	CYS	B	40	29.968	40.767	-3.775	1.00	42.46
B	C									
ATOM	1165	O	CYS	B	40	28.844	40.378	-4.077	1.00	42.43
B	O									
ATOM	1166	CB	CYS	B	40	29.771	42.107	-1.658	1.00	41.23
B	C									
ATOM	1167	SG	CYS	B	40	30.160	43.644	-0.756	1.00	38.48
B	S									
ATOM	1168	N	ARG	B	41	31.068	40.041	-3.980	1.00	42.65
B	N									
ATOM	1169	CA	ARG	B	41	31.038	38.705	-4.584	1.00	43.37
B	C									
ATOM	1170	CB	ARG	B	41	30.698	38.804	-6.076	1.00	44.07
B	C									
ATOM	1171	CG	ARG	B	41	30.800	37.482	-6.831	1.00	45.44
B	C									
ATOM	1172	CD	ARG	B	41	30.385	37.641	-8.290	1.00	46.08
B	C									
ATOM	1173	NE	ARG	B	41	30.473	36.388	-9.038	1.00	47.65
B	N									
ATOM	1174	CZ	ARG	B	41	31.612	35.781	-9.356	1.00	47.69
B	C									
ATOM	1175	NH1	ARG	B	41	32.774	36.307	-8.992	1.00	49.10
B	N									
ATOM	1176	NH2	ARG	B	41	31.590	34.646	-10.040	1.00	47.59
B	N									
ATOM	1177	C	ARG	B	41	32.390	38.014	-4.407	1.00	43.67
B	C									
ATOM	1178	O	ARG	B	41	33.417	38.683	-4.295	1.00	43.52
B	O									
ATOM	1179	N	LEU	B	42	32.381	36.682	-4.382	1.00	43.47
B	N									
ATOM	1180	CA	LEU	B	42	33.600	35.902	-4.210	1.00	44.42
B	C									
ATOM	1181	CB	LEU	B	42	33.695	35.356	-2.774	1.00	42.98
B	C									
ATOM	1182	CG	LEU	B	42	33.903	36.365	-1.643	1.00	41.64
B	C									
ATOM	1183	CD1	LEU	B	42	33.743	35.674	-0.299	1.00	41.04
B	C									
ATOM	1184	CD2	LEU	B	42	35.283	36.981	-1.768	1.00	40.35
B	C									
ATOM	1185	C	LEU	B	42	33.647	34.744	-5.195	1.00	45.72
B	C									

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ATOM	1186	O	LEU	B	42	32.635	34.098	-5.470	1.00	45.97
B	O									
ATOM	1187	N	ASP	B	43	34.834	34.483	-5.735	1.00	46.61
B	N									
ATOM	1188	CA	ASP	B	43	34.998	33.394	-6.693	1.00	47.21
B	C									
ATOM	1189	CB	AASP	B	43	36.396	33.446	-7.314	0.50	48.39
B	C									
ATOM	1190	CB	BASP	B	43	36.405	33.416	-7.276	0.50	48.20
B	C									
ATOM	1191	CG	AASP	B	43	36.566	32.454	-8.457	0.50	49.57
B	C									
ATOM	1192	CG	BASP	B	43	36.845	34.805	-7.676	0.50	49.13
B	C									
ATOM	1193	OD1AASP	B	43	35.827	32.564	-9.459	0.50	50.63	
B	O									
ATOM	1194	OD1BASP	B	43	37.622	35.414	-6.914	0.50	50.04	
B	O									
ATOM	1195	OD2AASP	B	43	37.432	31.557	-8.358	0.50	49.95	
B	O									
ATOM	1196	OD2BASP	B	43	36.422	35.282	-8.749	0.50	49.61	
B	O									
ATOM	1197	C	ASP	B	43	34.785	32.037	-6.023	1.00	47.20
B	C									
ATOM	1198	O	ASP	B	43	35.203	31.836	-4.884	1.00	46.97
B	O									
ATOM	1199	N	LYS	B	44	34.151	31.108	-6.736	1.00	47.14
B	N									
ATOM	1200	CA	LYS	B	44	33.869	29.771	-6.212	1.00	46.50
B	C									
ATOM	1201	CB	LYS	B	44	33.244	28.904	-7.310	1.00	48.36
B	C									
ATOM	1202	CG	LYS	B	44	31.876	29.408	-7.787	1.00	50.69
B	C									
ATOM	1203	CD	LYS	B	44	31.231	28.403	-8.735	1.00	52.34
B	C									
ATOM	1204	CE	LYS	B	44	29.832	28.829	-9.150	1.00	53.13
B	C									
ATOM	1205	NZ	LYS	B	44	29.175	27.806	-10.015	1.00	54.70
B	N									
ATOM	1206	C	LYS	B	44	35.121	29.094	-5.665	1.00	45.46
B	C									
ATOM	1207	O	LYS	B	44	35.083	28.353	-4.677	1.00	45.04
B	O									
ATOM	1208	N	SER	B	45	36.246	29.362	-6.314	1.00	44.73
B	N									
ATOM	1209	CA	SER	B	45	37.514	28.777	-5.899	1.00	44.17
B	C									
ATOM	1210	CB	ASER	B	45	38.659	29.317	-6.765	0.50	44.61
B	C									
ATOM	1211	CB	BSER	B	45	38.645	29.351	-6.767	0.50	44.45
B	C									
ATOM	1212	OG	ASER	B	45	39.915	28.799	-6.349	0.50	45.01
B	O									
ATOM	1213	OG	BSER	B	45	38.341	29.256	-8.145	0.50	44.34
B	O									
ATOM	1214	C	SER	B	45	37.828	29.037	-4.430	1.00	43.68
B	C									



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ATOM	1215	O	SER	B	45	38.358	28.164	-3.739	1.00	43.94
B	O									
ATOM	1216	N	ASN	B	46	37.504	30.237	-3.958	1.00	43.08
B	N									
ATOM	1217	CA	ASN	B	46	37.758	30.613	-2.573	1.00	41.72
B	C									
ATOM	1218	CB	ASN	B	46	37.229	32.023	-2.313	1.00	42.60
B	C									
ATOM	1219	CG	ASN	B	46	37.938	33.069	-3.134	1.00	42.66
B	C									
ATOM	1220	OD1	ASN	B	46	37.794	33.119	-4.353	1.00	43.85
B	O									
ATOM	1221	ND2	ASN	B	46	38.726	33.906	-2.471	1.00	43.52
B	N									
ATOM	1222	C	ASN	B	46	37.118	29.655	-1.569	1.00	40.56
B	C									
ATOM	1223	O	ASN	B	46	37.615	29.501	-0.457	1.00	40.87
B	O									
ATOM	1224	N	PHE	B	47	36.012	29.020	-1.949	1.00	39.67
B	N									
ATOM	1225	CA	PHE	B	47	35.319	28.103	-1.050	1.00	37.86
B	C									
ATOM	1226	CB	PHE	B	47	33.832	28.458	-1.007	1.00	37.18
B	C									
ATOM	1227	CG	PHE	B	47	33.549	29.753	-0.297	1.00	38.02
B	C									
ATOM	1228	CD1	PHE	B	47	33.520	29.807	1.093	1.00	37.75
B	C									
ATOM	1229	CD2	PHE	B	47	33.346	30.928	-1.017	1.00	37.55
B	C									
ATOM	1230	CE1	PHE	B	47	33.293	31.013	1.755	1.00	37.90
B	C									
ATOM	1231	CE2	PHE	B	47	33.120	32.137	-0.364	1.00	37.70
B	C									
ATOM	1232	CZ	PHE	B	47	33.094	32.179	1.024	1.00	37.15
B	C									
ATOM	1233	C	PHE	B	47	35.505	26.620	-1.365	1.00	38.38
B	C									
ATOM	1234	O	PHE	B	47	34.863	25.764	-0.758	1.00	39.24
B	O									
ATOM	1235	N	GLN	B	48	36.379	26.309	-2.313	1.00	37.58
B	N									
ATOM	1236	CA	GLN	B	48	36.642	24.915	-2.636	1.00	37.04
B	C									
ATOM	1237	CB	GLN	B	48	36.928	24.757	-4.129	1.00	38.28
B	C									
ATOM	1238	CG	GLN	B	48	35.687	24.947	-4.988	1.00	40.62
B	C									
ATOM	1239	CD	GLN	B	48	35.964	24.815	-6.471	1.00	41.52
B	C									
ATOM	1240	OE1	GLN	B	48	35.040	24.827	-7.284	1.00	42.61
B	O									
ATOM	1241	NE2	GLN	B	48	37.238	24.692	-6.832	1.00	42.47
B	N									
ATOM	1242	C	GLN	B	48	37.835	24.476	-1.793	1.00	35.19
B	C									
ATOM	1243	O	GLN	B	48	38.900	24.139	-2.307	1.00	35.18
B	O									

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ATOM	1244	N	GLN	B	49	37.635	24.504	-0.480	1.00	33.48
B	N									
ATOM	1245	CA	GLN	B	49	38.661	24.131	0.484	1.00	32.10
B	C									
ATOM	1246	CB	GLN	B	49	39.186	25.377	1.211	1.00	34.97
B	C									
ATOM	1247	CG	GLN	B	49	40.433	26.012	0.597	1.00	39.74
B	C									
ATOM	1248	CD	GLN	B	49	40.157	26.729	-0.707	1.00	42.56
B	C									
ATOM	1249	OE1	GLN	B	49	40.844	26.316	-1.768	1.00	44.68
B	O									
ATOM	1250	NE2	GLN	B	49	39.341	27.649	-0.760	1.00	44.50
B	N									
ATOM	1251	C	GLN	B	49	38.077	23.157	1.503	1.00	29.66
B	C									
ATOM	1252	O	GLN	B	49	37.583	23.569	2.556	1.00	28.91
B	O									
ATOM	1253	N	PRO	B	50	38.114	21.850	1.199	1.00	26.63
B	N									
ATOM	1254	CD	PRO	B	50	38.639	21.200	-0.013	1.00	26.53
B	C									
ATOM	1255	CA	PRO	B	50	37.570	20.860	2.134	1.00	24.12
B	C									
ATOM	1256	CB	PRO	B	50	37.720	19.541	1.375	1.00	26.35
B	C									
ATOM	1257	CG	PRO	B	50	38.902	19.796	0.468	1.00	26.74
B	C									
ATOM	1258	C	PRO	B	50	38.287	20.846	3.476	1.00	20.94
B	C									
ATOM	1259	O	PRO	B	50	37.652	20.728	4.522	1.00	20.16
B	O									
ATOM	1260	N	TYR	B	51	39.608	20.978	3.451	1.00	18.35
B	N									
ATOM	1261	CA	TYR	B	51	40.384	20.964	4.688	1.00	17.88
B	C									
ATOM	1262	CB	TYR	B	51	41.877	21.137	4.394	1.00	19.37
B	C									
ATOM	1263	CG	TYR	B	51	42.737	21.177	5.638	1.00	18.71
B	C									
ATOM	1264	CD1	TYR	B	51	43.015	20.014	6.352	1.00	19.74
B	C									
ATOM	1265	CE1	TYR	B	51	43.777	20.043	7.512	1.00	20.59
B	C									
ATOM	1266	CD2	TYR	B	51	43.250	22.385	6.118	1.00	20.02
B	C									
ATOM	1267	CE2	TYR	B	51	44.018	22.428	7.282	1.00	21.12
B	C									
ATOM	1268	CZ	TYR	B	51	44.274	21.253	7.973	1.00	22.10
B	C									
ATOM	1269	OH	TYR	B	51	45.008	21.287	9.137	1.00	24.61
B	O									
ATOM	1270	C	TYR	B	51	39.933	22.065	5.637	1.00	17.24
B	C									
ATOM	1271	O	TYR	B	51	39.560	21.793	6.773	1.00	17.29
B	O									
ATOM	1272	N	ILE	B	52	39.969	23.304	5.160	1.00	17.58
B	N									

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ATOM	1273	CA	ILE	B	52	39.571	24.448	5.973	1.00	21.11
B	C									
ATOM	1274	CB	ILE	B	52	39.827	25.760	5.210	1.00	24.48
B	C									
ATOM	1275	CG2	ILE	B	52	39.180	26.934	5.937	1.00	26.45
B	C									
ATOM	1276	CG1	ILE	B	52	41.342	25.956	5.062	1.00	26.38
B	C									
ATOM	1277	CD	ILE	B	52	41.748	27.215	4.340	1.00	31.77
B	C									
ATOM	1278	C	ILE	B	52	38.114	24.378	6.426	1.00	19.79
B	C									
ATOM	1279	O	ILE	B	52	37.782	24.812	7.530	1.00	20.54
B	O									
ATOM	1280	N	THR	B	53	37.246	23.834	5.579	1.00	18.58
B	N									
ATOM	1281	CA	THR	B	53	35.837	23.701	5.932	1.00	17.34
B	C									
ATOM	1282	CB	THR	B	53	35.032	23.103	4.765	1.00	19.54
B	C									
ATOM	1283	OG1	THR	B	53	35.186	23.939	3.610	1.00	21.25
B	O									
ATOM	1284	CG2	THR	B	53	33.558	23.017	5.121	1.00	18.98
B	C									
ATOM	1285	C	THR	B	53	35.732	22.782	7.146	1.00	16.46
B	C									
ATOM	1286	O	THR	B	53	35.092	23.116	8.139	1.00	17.44
B	O									
ATOM	1287	N	ASN	B	54	36.393	21.632	7.074	1.00	16.45
B	N									
ATOM	1288	CA	ASN	B	54	36.376	20.675	8.178	1.00	15.65
B	C									
ATOM	1289	CB	ASN	B	54	37.164	19.413	7.806	1.00	17.11
B	C									
ATOM	1290	CG	ASN	B	54	36.359	18.455	6.942	1.00	19.54
B	C									
ATOM	1291	OD1	ASN	B	54	35.337	18.827	6.372	1.00	19.10
B	O									
ATOM	1292	ND2	ASN	B	54	36.826	17.221	6.835	1.00	20.54
B	N									
ATOM	1293	C	ASN	B	54	36.969	21.288	9.441	1.00	16.14
B	C									
ATOM	1294	O	ASN	B	54	36.422	21.134	10.535	1.00	16.51
B	O									
ATOM	1295	N	ARG	B	55	38.087	21.990	9.284	1.00	16.11
B	N									
ATOM	1296	CA	ARG	B	55	38.748	22.618	10.425	1.00	16.50
B	C									
ATOM	1297	CB	AARG	B	55	40.100	23.214	10.006	0.50	18.63
B	C									
ATOM	1298	CB	BARG	B	55	40.069	23.223	10.002	0.50	18.75
B	C									
ATOM	1299	CG	AARG	B	55	41.043	22.199	9.379	0.50	22.49
B	C									
ATOM	1300	CG	BARG	B	55	41.066	22.263	9.348	0.50	22.67
B	C									
ATOM	1301	CD	AARG	B	55	41.300	21.017	10.307	0.50	25.57
B	C									

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ATOM B	1302	CD	BARG	B	55	41.866	21.447	10.363	0.50	26.03
ATOM B	1303	NE	AARG	B	55	42.403	21.236	11.238	0.50	28.75
ATOM B	1304	NE	BARG	B	55	41.176	20.260	10.872	0.50	28.52
ATOM B	1305	CZ	AARG	B	55	42.799	20.343	12.141	0.50	30.20
ATOM B	1306	CZ	BARG	B	55	41.716	19.416	11.751	0.50	30.40
ATOM B	1307	NH1A	AARG	B	55	42.180	19.173	12.241	0.50	32.50
ATOM B	1308	NH1B	AARG	B	55	42.935	19.643	12.215	0.50	31.14
ATOM B	1309	NH2A	AARG	B	55	43.825	20.611	12.935	0.50	31.35
ATOM B	1310	NH2B	AARG	B	55	41.066	18.325	12.142	0.50	30.17
ATOM B	1311	C	ARG	B	55	37.883	23.712	11.041	1.00	13.93
ATOM B	1312	O	ARG	B	55	37.924	23.939	12.252	1.00	13.25
ATOM B	1313	N	THR	B	56	37.100	24.392	10.208	1.00	14.26
ATOM B	1314	CA	THR	B	56	36.230	25.452	10.693	1.00	11.34
ATOM B	1315	CB	THR	B	56	35.585	26.237	9.525	1.00	14.38
ATOM B	1316	OG1	THR	B	56	36.614	26.908	8.779	1.00	14.44
ATOM B	1317	CG2	THR	B	56	34.587	27.266	10.052	1.00	11.15
ATOM B	1318	C	THR	B	56	35.149	24.817	11.556	1.00	13.75
ATOM B	1319	O	THR	B	56	34.817	25.319	12.631	1.00	14.25
ATOM B	1320	N	PHE	B	57	34.598	23.700	11.089	1.00	13.72
ATOM B	1321	CA	PHE	B	57	33.565	23.018	11.851	1.00	13.15
ATOM B	1322	CB	PHE	B	57	32.899	21.932	11.001	1.00	13.02
ATOM B	1323	CG	PHE	B	57	31.799	22.453	10.117	1.00	11.26
ATOM B	1324	CD1	PHE	B	57	32.085	23.289	9.044	1.00	12.61
ATOM B	1325	CD2	PHE	B	57	30.472	22.125	10.377	1.00	11.56
ATOM B	1326	CE1	PHE	B	57	31.069	23.792	8.241	1.00	14.35
ATOM B	1327	CE2	PHE	B	57	29.443	22.621	9.582	1.00	11.35
ATOM B	1328	CZ	PHE	B	57	29.741	23.458	8.509	1.00	11.81
ATOM B	1329	C	PHE	B	57	34.138	22.431	13.142	1.00	13.86
ATOM B	1330	O	PHE	B	57	33.444	22.354	14.153	1.00	14.13

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ATOM	1331	N	MET	B	58	35.405	22.029	13.124	1.00	15.45
B	N									
ATOM	1332	CA	MET	B	58	36.004	21.481	14.335	1.00	16.62
B	C									
ATOM	1333	CB	MET	B	58	37.325	20.792	14.017	1.00	21.38
B	C									
ATOM	1334	CG	MET	B	58	37.130	19.435	13.368	1.00	27.49
B	C									
ATOM	1335	SD	MET	B	58	36.220	18.220	14.333	1.00	33.41
B	S									
ATOM	1336	CE	MET	B	58	37.378	17.916	15.662	1.00	29.95
B	C									
ATOM	1337	C	MET	B	58	36.221	22.601	15.343	1.00	15.87
B	C									
ATOM	1338	O	MET	B	58	36.000	22.429	16.538	1.00	14.52
B	O									
ATOM	1339	N	LEU	B	59	36.652	23.755	14.852	1.00	14.79
B	N									
ATOM	1340	CA	LEU	B	59	36.871	24.898	15.719	1.00	13.60
B	C									
ATOM	1341	CB	LEU	B	59	37.416	26.076	14.910	1.00	12.59
B	C									
ATOM	1342	CG	LEU	B	59	37.506	27.417	15.643	1.00	12.48
B	C									
ATOM	1343	CD1	LEU	B	59	38.352	27.260	16.896	1.00	13.58
B	C									
ATOM	1344	CD2	LEU	B	59	38.105	28.476	14.710	1.00	11.97
B	C									
ATOM	1345	C	LEU	B	59	35.540	25.283	16.364	1.00	13.10
B	C									
ATOM	1346	O	LEU	B	59	35.480	25.538	17.566	1.00	14.28
B	O									
ATOM	1347	N	ALA	B	60	34.477	25.325	15.558	1.00	11.11
B	N									
ATOM	1348	CA	ALA	B	60	33.145	25.670	16.055	1.00	12.18
B	C									
ATOM	1349	CB	ALA	B	60	32.148	25.744	14.879	1.00	11.09
B	C									
ATOM	1350	C	ALA	B	60	32.665	24.659	17.103	1.00	12.00
B	C									
ATOM	1351	O	ALA	B	60	32.070	25.031	18.119	1.00	9.58
B	O									
ATOM	1352	N	LYS	B	61	32.915	23.376	16.863	1.00	12.27
B	N									
ATOM	1353	CA	LYS	B	61	32.515	22.351	17.818	1.00	13.95
B	C									
ATOM	1354	CB	LYS	B	61	32.842	20.952	17.294	1.00	14.14
B	C									
ATOM	1355	CG	LYS	B	61	31.862	20.412	16.282	1.00	19.93
B	C									
ATOM	1356	CD	LYS	B	61	32.281	19.014	15.841	1.00	19.80
B	C									
ATOM	1357	CE	LYS	B	61	31.339	18.454	14.799	1.00	23.77
B	C									
ATOM	1358	NZ	LYS	B	61	32.028	17.403	14.007	1.00	22.83
B	N									
ATOM	1359	C	LYS	B	61	33.228	22.534	19.143	1.00	13.07
B	C									

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ATOM	1360	O	LYS	B	61	32.611	22.446	20.203	1.00	13.89
B	O									
ATOM	1361	N	GLU	B	62	34.532	22.782	19.079	1.00	12.95
B	N									
ATOM	1362	CA	GLU	B	62	35.335	22.955	20.289	1.00	13.90
B	C									
ATOM	1363	CB	GLU	B	62	36.804	23.164	19.906	1.00	15.80
B	C									
ATOM	1364	CG	GLU	B	62	37.756	23.426	21.071	1.00	19.60
B	C									
ATOM	1365	CD	GLU	B	62	37.749	22.321	22.122	1.00	23.26
B	C									
ATOM	1366	OE1	GLU	B	62	37.759	21.127	21.747	1.00	23.30
B	O									
ATOM	1367	OE2	GLU	B	62	37.746	22.654	23.332	1.00	25.11
B	O									
ATOM	1368	C	GLU	B	62	34.841	24.116	21.137	1.00	13.12
B	C									
ATOM	1369	O	GLU	B	62	34.654	23.974	22.346	1.00	15.86
B	O									
ATOM	1370	N	ALA	B	63	34.638	25.269	20.509	1.00	12.37
B	N									
ATOM	1371	CA	ALA	B	63	34.164	26.444	21.228	1.00	11.98
B	C									
ATOM	1372	CB	ALA	B	63	34.214	27.674	20.322	1.00	10.58
B	C									
ATOM	1373	C	ALA	B	63	32.743	26.220	21.732	1.00	12.40
B	C									
ATOM	1374	O	ALA	B	63	32.383	26.695	22.802	1.00	14.78
B	O									
ATOM	1375	N	SER	B	64	31.938	25.487	20.967	1.00	13.59
B	N									
ATOM	1376	CA	SER	B	64	30.557	25.225	21.361	1.00	14.14
B	C									
ATOM	1377	CB	SER	B	64	29.825	24.450	20.266	1.00	13.79
B	C									
ATOM	1378	OG	SER	B	64	29.537	25.295	19.166	1.00	15.71
B	O									
ATOM	1379	C	SER	B	64	30.464	24.468	22.680	1.00	16.02
B	C									
ATOM	1380	O	SER	B	64	29.456	24.576	23.389	1.00	14.81
B	O									
ATOM	1381	N	LEU	B	65	31.516	23.715	23.009	1.00	16.10
B	N									
ATOM	1382	CA	LEU	B	65	31.546	22.951	24.258	1.00	18.41
B	C									
ATOM	1383	CB	LEU	B	65	32.829	22.124	24.362	1.00	19.27
B	C									
ATOM	1384	CG	LEU	B	65	33.084	21.082	23.277	1.00	19.94
B	C									
ATOM	1385	CD1	LEU	B	65	34.420	20.401	23.556	1.00	21.12
B	C									
ATOM	1386	CD2	LEU	B	65	31.941	20.069	23.233	1.00	19.85
B	C									
ATOM	1387	C	LEU	B	65	31.461	23.873	25.472	1.00	21.28
B	C									
ATOM	1388	O	LEU	B	65	30.913	23.496	26.508	1.00	20.85
B	O									

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ATOM	1389	N	ALA	B	66	31.993	25.084	25.337	1.00	22.77
B	N									
ATOM	1390	CA	ALA	B	66	31.991	26.041	26.440	1.00	23.05
B	C									
ATOM	1391	CB	ALA	B	66	33.340	26.759	26.505	1.00	23.03
B	C									
ATOM	1392	C	ALA	B	66	30.864	27.063	26.349	1.00	25.33
B	C									
ATOM	1393	O	ALA	B	66	30.794	27.989	27.160	1.00	24.62
B	O									
ATOM	1394	N	ASP	B	67	29.984	26.895	25.366	1.00	24.71
B	N									
ATOM	1395	CA	ASP	B	67	28.859	27.805	25.169	1.00	24.59
B	C									
ATOM	1396	CB	ASP	B	67	28.843	28.293	23.715	1.00	21.80
B	C									
ATOM	1397	CG	ASP	B	67	27.658	29.193	23.409	1.00	23.11
B	C									
ATOM	1398	OD1	ASP	B	67	27.492	30.220	24.101	1.00	21.79
B	O									
ATOM	1399	OD2	ASP	B	67	26.894	28.881	22.468	1.00	22.86
B	O									
ATOM	1400	C	ASP	B	67	27.539	27.105	25.484	1.00	24.11
B	C									
ATOM	1401	O	ASP	B	67	27.339	25.961	25.090	1.00	24.85
B	O									
ATOM	1402	N	ASN	B	68	26.643	27.781	26.199	1.00	23.66
B	N									
ATOM	1403	CA	ASN	B	68	25.341	27.190	26.505	1.00	26.10
B	C									
ATOM	1404	CB	ASN	B	68	24.606	27.991	27.584	1.00	26.12
B	C									
ATOM	1405	CG	ASN	B	68	23.178	27.507	27.791	1.00	28.10
B	C									
ATOM	1406	OD1	ASN	B	68	22.902	26.309	27.704	1.00	30.31
B	O									
ATOM	1407	ND2	ASN	B	68	22.267	28.432	28.075	1.00	29.58
B	N									
ATOM	1408	C	ASN	B	68	24.514	27.191	25.223	1.00	26.09
B	C									
ATOM	1409	O	ASN	B	68	24.122	28.252	24.733	1.00	25.01
B	O									
ATOM	1410	N	ASN	B	69	24.245	26.006	24.682	1.00	26.55
B	N									
ATOM	1411	CA	ASN	B	69	23.488	25.905	23.435	1.00	28.23
B	C									
ATOM	1412	CB	ASN	B	69	23.321	24.443	23.029	1.00	29.69
B	C									
ATOM	1413	CG	ASN	B	69	24.642	23.743	22.885	1.00	32.95
B	C									
ATOM	1414	OD1	ASN	B	69	25.616	24.339	22.428	1.00	33.35
B	O									
ATOM	1415	ND2	ASN	B	69	24.690	22.470	23.268	1.00	35.41
B	N									
ATOM	1416	C	ASN	B	69	22.129	26.575	23.462	1.00	27.38
B	C									
ATOM	1417	O	ASN	B	69	21.754	27.280	22.527	1.00	26.91
B	O									

ATOM	1418	N	THR	B	70	21.386	26.367	24.533	1.00	27.43
B	N									
ATOM	1419	CA	THR	B	70	20.063	26.963	24.620	1.00	31.14
B	C									
ATOM	1420	CB	THR	B	70	19.290	26.312	25.724	1.00	33.84
B	C									
ATOM	1421	OG1	THR	B	70	20.017	26.483	26.949	1.00	38.79
B	O									
ATOM	1422	CG2	THR	B	70	19.099	24.825	25.414	1.00	35.38
B	C									
ATOM	1423	C	THR	B	70	20.084	28.472	24.850	1.00	29.99
B	C									
ATOM	1424	O	THR	B	70	19.032	29.100	24.983	1.00	31.80
B	O									
ATOM	1425	N	ASP	B	71	21.280	29.048	24.900	1.00	28.37
B	N									
ATOM	1426	CA	ASP	B	71	21.420	30.481	25.102	1.00	25.20
B	C									
ATOM	1427	CB	ASP	B	71	22.838	30.798	25.589	1.00	24.99
B	C									
ATOM	1428	CG	ASP	B	71	22.995	32.241	26.019	1.00	25.37
B	C									
ATOM	1429	OD1	ASP	B	71	21.991	32.842	26.457	1.00	24.56
B	O									
ATOM	1430	OD2	ASP	B	71	24.120	32.775	25.929	1.00	24.43
B	O									
ATOM	1431	C	ASP	B	71	21.124	31.210	23.789	1.00	24.70
B	C									
ATOM	1432	O	ASP	B	71	20.958	30.579	22.741	1.00	25.80
B	O									
ATOM	1433	N	VAL	B	72	21.051	32.536	23.852	1.00	22.24
B	N									
ATOM	1434	CA	VAL	B	72	20.769	33.352	22.674	1.00	21.58
B	C									
ATOM	1435	CB	VAL	B	72	20.887	34.856	23.015	1.00	21.53
B	C									
ATOM	1436	CG1	VAL	B	72	22.310	35.177	23.443	1.00	21.59
B	C									
ATOM	1437	CG2	VAL	B	72	20.468	35.711	21.818	1.00	24.37
B	C									
ATOM	1438	C	VAL	B	72	21.729	33.005	21.534	1.00	21.11
B	C									
ATOM	1439	O	VAL	B	72	22.864	32.600	21.773	1.00	17.71
B	O									
ATOM	1440	N	ARG	B	73	21.259	33.162	20.300	1.00	19.03
B	N									
ATOM	1441	CA	ARG	B	73	22.062	32.861	19.120	1.00	21.00
B	C									
ATOM	1442	CB	ARG	B	73	21.242	32.005	18.145	1.00	20.05
B	C									
ATOM	1443	CG	ARG	B	73	20.914	30.607	18.658	1.00	22.93
B	C									
ATOM	1444	CD	ARG	B	73	22.184	29.788	18.848	1.00	23.32
B	C									
ATOM	1445	NE	ARG	B	73	22.541	29.607	20.253	1.00	26.02
B	N									
ATOM	1446	CZ	ARG	B	73	23.792	29.534	20.701	1.00	28.62
B	C									



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ATOM	1447	NH1	ARG	B	73	24.810	29.643	19.850	1.00	27.83
B	N									
ATOM	1448	NH2	ARG	B	73	24.032	29.318	21.991	1.00	24.28
B	N									
ATOM	1449	C	ARG	B	73	22.562	34.130	18.422	1.00	19.92
B	C									
ATOM	1450	O	ARG	B	73	22.231	35.242	18.823	1.00	23.35
B	O									
ATOM	1451	N	LEU	B	74	23.361	33.956	17.375	1.00	18.84
B	N									
ATOM	1452	CA	LEU	B	74	23.928	35.091	16.644	1.00	18.10
B	C									
ATOM	1453	CB	LEU	B	74	25.452	35.071	16.764	1.00	17.88
B	C									
ATOM	1454	CG	LEU	B	74	26.021	35.213	18.178	1.00	17.88
B	C									
ATOM	1455	CD1	LEU	B	74	27.514	34.966	18.146	1.00	19.62
B	C									
ATOM	1456	CD2	LEU	B	74	25.711	36.602	18.727	1.00	16.68
B	C									
ATOM	1457	C	LEU	B	74	23.550	35.113	15.172	1.00	18.69
B	C									
ATOM	1458	O	LEU	B	74	22.990	36.094	14.678	1.00	17.25
B	O									
ATOM	1459	N	ILE	B	75	23.864	34.026	14.478	1.00	18.86
B	N									
ATOM	1460	CA	ILE	B	75	23.565	33.900	13.055	1.00	19.94
B	C									
ATOM	1461	CB	AILE	B	75	24.683	33.133	12.315	0.50	19.70
B	C									
ATOM	1462	CB	BILE	B	75	24.685	33.159	12.306	0.50	19.21
B	C									
ATOM	1463	CG2AILE	B	75	24.354	33.044	10.830	0.50	20.21	
B	C									
ATOM	1464	CG2BILE	B	75	24.280	32.922	10.857	0.50	19.75	
B	C									
ATOM	1465	CG1AILE	B	75	26.032	33.829	12.533	0.50	21.96	
B	C									
ATOM	1466	CG1BILE	B	75	25.976	33.983	12.354	0.50	20.78	
B	C									
ATOM	1467	CD	AILE	B	75	26.075	35.259	12.036	0.50	21.49
B	C									
ATOM	1468	CD	BILE	B	75	27.167	33.330	11.684	0.50	19.44
B	C									
ATOM	1469	C	ILE	B	75	22.250	33.159	12.850	1.00	19.75
B	C									
ATOM	1470	O	ILE	B	75	22.118	32.001	13.241	1.00	19.53
B	O									
ATOM	1471	N	GLY	B	76	21.279	33.834	12.244	1.00	20.72
B	N									
ATOM	1472	CA	GLY	B	76	19.991	33.215	12.002	1.00	21.85
B	C									
ATOM	1473	C	GLY	B	76	19.144	34.080	11.090	1.00	23.94
B	C									
ATOM	1474	O	GLY	B	76	19.583	35.137	10.625	1.00	21.15
B	O									
ATOM	1475	N	GLU	B	77	17.915	33.637	10.849	1.00	24.76
B	N									

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ATOM	1476	CA	GLU	B	77	16.994	34.355	9.981	1.00	25.59
B	C									
ATOM	1477	CB	GLU	B	77	15.622	33.683	10.024	1.00	28.23
B	C									
ATOM	1478	CG	GLU	B	77	14.939	33.702	11.385	1.00	29.97
B	C									
ATOM	1479	CD	GLU	B	77	14.300	35.043	11.702	1.00	31.49
B	C									
ATOM	1480	OE1	GLU	B	77	13.646	35.618	10.805	1.00	31.82
B	O									
ATOM	1481	OE2	GLU	B	77	14.438	35.516	12.851	1.00	32.75
B	O									
ATOM	1482	C	GLU	B	77	16.863	35.826	10.340	1.00	26.42
B	C									
ATOM	1483	O	GLU	B	77	16.733	36.667	9.454	1.00	25.64
B	O									
ATOM	1484	N	LYS	B	78	16.903	36.141	11.632	1.00	26.48
B	N									
ATOM	1485	CA	LYS	B	78	16.769	37.529	12.071	1.00	26.66
B	C									
ATOM	1486	CB	LYS	B	78	16.769	37.614	13.607	1.00	29.51
B	C									
ATOM	1487	CG	LYS	B	78	17.949	36.911	14.306	1.00	34.38
B	C									
ATOM	1488	CD	LYS	B	78	17.866	35.363	14.172	1.00	34.31
B	C									
ATOM	1489	CE	LYS	B	78	19.033	34.584	14.838	1.00	35.41
B	C									
ATOM	1490	NZ	LYS	B	78	19.360	35.086	16.206	1.00	33.27
B	N									
ATOM	1491	C	LYS	B	78	17.845	38.439	11.488	1.00	25.68
B	C									
ATOM	1492	O	LYS	B	78	17.585	39.607	11.182	1.00	25.09
B	O									
ATOM	1493	N	LEU	B	79	19.049	37.903	11.322	1.00	22.46
B	N									
ATOM	1494	CA	LEU	B	79	20.158	38.663	10.759	1.00	22.51
B	C									
ATOM	1495	CB	LEU	B	79	21.421	37.790	10.744	1.00	21.91
B	C									
ATOM	1496	CG	LEU	B	79	22.765	38.360	10.272	1.00	21.91
B	C									
ATOM	1497	CD1	LEU	B	79	23.199	39.526	11.164	1.00	20.83
B	C									
ATOM	1498	CD2	LEU	B	79	23.819	37.255	10.317	1.00	18.82
B	C									
ATOM	1499	C	LEU	B	79	19.833	39.125	9.332	1.00	23.76
B	C									
ATOM	1500	O	LEU	B	79	20.355	40.139	8.858	1.00	21.25
B	O									
ATOM	1501	N	PHE	B	80	18.957	38.389	8.655	1.00	23.14
B	N									
ATOM	1502	CA	PHE	B	80	18.605	38.721	7.283	1.00	24.04
B	C									
ATOM	1503	CB	PHE	B	80	18.576	37.448	6.434	1.00	22.67
B	C									
ATOM	1504	CG	PHE	B	80	19.852	36.665	6.484	1.00	22.24
B	C									

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ATOM	1505	CD1	PHE	B	80	20.086	35.754	7.508	1.00	22.35
B	C									
ATOM	1506	CD2	PHE	B	80	20.837	36.863	5.527	1.00	22.73
B	C									
ATOM	1507	CE1	PHE	B	80	21.286	35.051	7.578	1.00	23.09
B	C									
ATOM	1508	CE2	PHE	B	80	22.039	36.164	5.591	1.00	24.92
B	C									
ATOM	1509	CZ	PHE	B	80	22.262	35.255	6.622	1.00	23.28
B	C									
ATOM	1510	C	PHE	B	80	17.289	39.474	7.113	1.00	25.53
B	C									
ATOM	1511	O	PHE	B	80	16.817	39.650	5.989	1.00	25.25
B	O									
ATOM	1512	N	HIS	B	81	16.705	39.928	8.218	1.00	26.38
B	N									
ATOM	1513	CA	HIS	B	81	15.444	40.662	8.192	1.00	27.94
B	C									
ATOM	1514	CB	AHIS	B	81	15.100	41.146	9.593	0.50	31.29
B	C									
ATOM	1515	CB	BHIS	B	81	15.009	41.082	9.560	0.50	31.04
B	C									
ATOM	1516	CG	AHIS	B	81	13.748	41.770	9.701	0.50	34.69
B	C									
ATOM	1517	CG	BHIS	B	81	14.361	40.000	10.367	0.50	33.94
B	C									
ATOM	1518	CD2AHIS	B	81	12.617	41.581	8.966	0.50	35.93	
B	C									
ATOM	1519	CD2BHIS	B	81	14.072	38.713	10.063	0.50	35.25	
B	C									
ATOM	1520	ND1AHIS	B	81	13.422	42.706	10.655	0.50	36.16	
B	N									
ATOM	1521	ND1BHIS	B	81	13.923	40.196	11.660	0.50	35.74	
B	N									
ATOM	1522	CE1AHIS	B	81	12.158	43.070	10.511	0.50	37.27	
B	C									
ATOM	1523	CE1BHIS	B	81	13.393	39.075	12.117	0.50	36.86	
B	C									
ATOM	1524	NE2AHIS	B	81	11.653	42.400	9.493	0.50	37.17	
B	N									
ATOM	1525	NE2BHIS	B	81	13.470	38.160	11.168	0.50	36.06	
B	N									
ATOM	1526	C	HIS	B	81	15.507	41.870	7.260	1.00	27.52
B	C									
ATOM	1527	O	HIS	B	81	16.309	42.781	7.473	1.00	27.00
B	O									
ATOM	1528	N	GLY	B	82	14.685	41.857	6.213	1.00	26.26
B	N									
ATOM	1529	CA	GLY	B	82	14.667	42.960	5.270	1.00	24.51
B	C									
ATOM	1530	C	GLY	B	82	15.874	43.081	4.366	1.00	24.60
B	C									
ATOM	1531	O	GLY	B	82	16.060	44.108	3.722	1.00	25.03
B	O									
ATOM	1532	N	VAL	B	83	16.702	42.044	4.317	1.00	26.22
B	N									
ATOM	1533	CA	VAL	B	83	17.894	42.058	3.474	1.00	24.22
B	C									

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ATOM	1534	CB	VAL	B	83	19.099	41.422	4.198	1.00	23.59
B	C									
ATOM	1535	CG1	VAL	B	83	20.338	41.501	3.315	1.00	21.40
B	C									
ATOM	1536	CG2	VAL	B	83	19.332	42.121	5.526	1.00	20.96
B	C									
ATOM	1537	C	VAL	B	83	17.635	41.282	2.188	1.00	26.23
B	C									
ATOM	1538	O	VAL	B	83	17.400	40.078	2.220	1.00	26.03
B	O									
ATOM	1539	N	SER	B	84	17.671	41.974	1.055	1.00	29.00
B	N									
ATOM	1540	CA	SER	B	84	17.438	41.317	-0.226	1.00	31.27
B	C									
ATOM	1541	CB	SER	B	84	17.307	42.360	-1.341	1.00	31.72
B	C									
ATOM	1542	OG	SER	B	84	18.503	43.103	-1.500	1.00	34.12
B	O									
ATOM	1543	C	SER	B	84	18.599	40.374	-0.522	1.00	32.20
B	C									
ATOM	1544	O	SER	B	84	19.659	40.476	0.099	1.00	31.68
B	O									
ATOM	1545	N	MET	B	85	18.396	39.454	-1.462	1.00	32.77
B	N									
ATOM	1546	CA	MET	B	85	19.434	38.492	-1.837	1.00	33.78
B	C									
ATOM	1547	CB	MET	B	85	18.916	37.542	-2.925	1.00	36.68
B	C									
ATOM	1548	CG	MET	B	85	17.883	36.545	-2.439	1.00	40.28
B	C									
ATOM	1549	SD	MET	B	85	18.469	35.551	-1.056	1.00	48.72
B	S									
ATOM	1550	CE	MET	B	85	19.962	34.852	-1.742	1.00	44.99
B	C									
ATOM	1551	C	MET	B	85	20.704	39.167	-2.342	1.00	32.27
B	C									
ATOM	1552	O	MET	B	85	21.814	38.650	-2.165	1.00	33.11
B	O									
ATOM	1553	N	SER	B	86	20.538	40.323	-2.971	1.00	30.58
B	N									
ATOM	1554	CA	SER	B	86	21.669	41.053	-3.521	1.00	31.46
B	C									
ATOM	1555	CB	SER	B	86	21.187	42.065	-4.573	1.00	32.63
B	C									
ATOM	1556	OG	SER	B	86	20.319	43.052	-4.031	1.00	39.50
B	O									
ATOM	1557	C	SER	B	86	22.492	41.774	-2.471	1.00	29.04
B	C									
ATOM	1558	O	SER	B	86	23.608	42.227	-2.746	1.00	28.91
B	O									
ATOM	1559	N	GLU	B	87	21.941	41.863	-1.265	1.00	26.59
B	N									
ATOM	1560	CA	GLU	B	87	22.608	42.539	-0.162	1.00	24.76
B	C									
ATOM	1561	CB	GLU	B	87	21.601	43.420	0.581	1.00	25.49
B	C									
ATOM	1562	CG	GLU	B	87	20.847	44.392	-0.313	1.00	29.17
B	C									

ATOM	1563	CD	GLU	B	87	19.853	45.248	0.449	1.00	30.87
B	C									
ATOM	1564	OE1	GLU	B	87	19.028	44.689	1.206	1.00	30.33
B	O									
ATOM	1565	OE2	GLU	B	87	19.891	46.484	0.283	1.00	35.00
B	O									
ATOM	1566	C	GLU	B	87	23.257	41.563	0.821	1.00	23.73
B	C									
ATOM	1567	O	GLU	B	87	24.029	41.972	1.685	1.00	21.32
B	O									
ATOM	1568	N	ARG	B	88	22.957	40.276	0.676	1.00	22.70
B	N									
ATOM	1569	CA	ARG	B	88	23.499	39.261	1.578	1.00	24.54
B	C									
ATOM	1570	CB	ARG	B	88	22.967	37.881	1.194	1.00	25.66
B	C									
ATOM	1571	CG	ARG	B	88	21.509	37.681	1.537	1.00	27.47
B	C									
ATOM	1572	CD	ARG	B	88	21.118	36.224	1.391	1.00	29.90
B	C									
ATOM	1573	NE	ARG	B	88	19.755	35.977	1.853	1.00	33.50
B	N									
ATOM	1574	CZ	ARG	B	88	19.197	34.772	1.926	1.00	34.03
B	C									
ATOM	1575	NH1	ARG	B	88	19.888	33.699	1.569	1.00	34.95
B	N									
ATOM	1576	NH2	ARG	B	88	17.947	34.642	2.350	1.00	35.52
B	N									
ATOM	1577	C	ARG	B	88	25.018	39.187	1.727	1.00	23.31
B	C									
ATOM	1578	O	ARG	B	88	25.522	39.058	2.841	1.00	23.06
B	O									
ATOM	1579	N	CYS	B	89	25.756	39.256	0.626	1.00	23.32
B	N									
ATOM	1580	CA	CYS	B	89	27.208	39.170	0.739	1.00	22.87
B	C									
ATOM	1581	C	CYS	B	89	27.778	40.378	1.486	1.00	22.34
B	C									
ATOM	1582	O	CYS	B	89	28.706	40.238	2.287	1.00	20.71
B	O									
ATOM	1583	CB	CYS	B	89	27.865	39.037	-0.639	1.00	22.30
B	C									
ATOM	1584	SG	CYS	B	89	29.668	38.836	-0.507	1.00	24.58
B	S									
ATOM	1585	N	TYR	B	90	27.207	41.555	1.232	1.00	22.12
B	N									
ATOM	1586	CA	TYR	B	90	27.636	42.786	1.891	1.00	21.33
B	C									
ATOM	1587	CB	TYR	B	90	26.896	43.990	1.307	1.00	24.19
B	C									
ATOM	1588	CG	TYR	B	90	27.227	45.299	1.989	1.00	25.69
B	C									
ATOM	1589	CD1	TYR	B	90	28.484	45.897	1.838	1.00	26.69
B	C									
ATOM	1590	CE1	TYR	B	90	28.795	47.101	2.483	1.00	26.25
B	C									
ATOM	1591	CD2	TYR	B	90	26.290	45.933	2.803	1.00	26.17
B	C									

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ATOM	1592	CE2	TYR	B	90	26.591	47.130	3.452	1.00	27.02
B	C									
ATOM	1593	CZ	TYR	B	90	27.842	47.707	3.288	1.00	26.75
B	C									
ATOM	1594	OH	TYR	B	90	28.129	48.891	3.925	1.00	28.36
B	O									
ATOM	1595	C	TYR	B	90	27.310	42.652	3.375	1.00	20.94
B	C									
ATOM	1596	O	TYR	B	90	28.081	43.075	4.239	1.00	21.09
B	O									
ATOM	1597	N	LEU	B	91	26.156	42.065	3.658	1.00	17.63
B	N									
ATOM	1598	CA	LEU	B	91	25.724	41.828	5.031	1.00	18.40
B	C									
ATOM	1599	CB	LEU	B	91	24.349	41.158	5.025	1.00	19.21
B	C									
ATOM	1600	CG	LEU	B	91	23.874	40.595	6.361	1.00	22.33
B	C									
ATOM	1601	CD1	LEU	B	91	23.538	41.736	7.296	1.00	19.22
B	C									
ATOM	1602	CD2	LEU	B	91	22.657	39.700	6.137	1.00	23.86
B	C									
ATOM	1603	C	LEU	B	91	26.734	40.912	5.741	1.00	17.20
B	C									
ATOM	1604	O	LEU	B	91	27.210	41.211	6.841	1.00	17.10
B	O									
ATOM	1605	N	MET	B	92	27.056	39.791	5.107	1.00	16.43
B	N									
ATOM	1606	CA	MET	B	92	27.997	38.847	5.685	1.00	17.07
B	C									
ATOM	1607	CB	MET	B	92	28.002	37.552	4.871	1.00	16.48
B	C									
ATOM	1608	CG	MET	B	92	26.703	36.752	4.979	1.00	17.63
B	C									
ATOM	1609	SD	MET	B	92	26.128	36.605	6.690	1.00	17.99
B	S									
ATOM	1610	CE	MET	B	92	27.492	35.700	7.425	1.00	14.17
B	C									
ATOM	1611	C	MET	B	92	29.410	39.430	5.790	1.00	18.87
B	C									
ATOM	1612	O	MET	B	92	30.187	39.048	6.670	1.00	17.61
B	O									
ATOM	1613	N	LYS	B	93	29.747	40.350	4.891	1.00	20.69
B	N									
ATOM	1614	CA	LYS	B	93	31.060	40.988	4.936	1.00	20.45
B	C									
ATOM	1615	CB	LYS	B	93	31.219	41.984	3.791	1.00	21.79
B	C									
ATOM	1616	CG	LYS	B	93	32.527	42.755	3.838	1.00	22.89
B	C									
ATOM	1617	CD	LYS	B	93	32.490	43.949	2.892	1.00	27.03
B	C									
ATOM	1618	CE	LYS	B	93	33.765	44.778	2.995	1.00	28.50
B	C									
ATOM	1619	NZ	LYS	B	93	33.700	46.001	2.138	1.00	30.45
B	N									
ATOM	1620	C	LYS	B	93	31.181	41.732	6.267	1.00	19.66
B	C									

ATOM	1621	O	LYS	B	93	32.200	41.649	6.946	1.00	19.17
B	O									
ATOM	1622	N	GLN	B	94	30.131	42.456	6.637	1.00	19.14
B	N									
ATOM	1623	CA	GLN	B	94	30.136	43.201	7.890	1.00	19.70
B	C									
ATOM	1624	CB	GLN	B	94	28.814	43.956	8.061	1.00	21.16
B	C									
ATOM	1625	CG	GLN	B	94	28.392	44.765	6.844	1.00	22.73
B	C									
ATOM	1626	CD	GLN	B	94	29.451	45.752	6.397	1.00	22.05
B	C									
ATOM	1627	OE1	GLN	B	94	29.802	45.806	5.217	1.00	26.54
B	O									
ATOM	1628	NE2	GLN	B	94	29.963	46.541	7.333	1.00	18.51
B	N									
ATOM	1629	C	GLN	B	94	30.329	42.244	9.071	1.00	18.12
B	C									
ATOM	1630	O	GLN	B	94	31.121	42.510	9.980	1.00	17.93
B	O									
ATOM	1631	N	VAL	B	95	29.592	41.138	9.055	1.00	14.83
B	N									
ATOM	1632	CA	VAL	B	95	29.679	40.140	10.117	1.00	13.76
B	C									
ATOM	1633	CB	VAL	B	95	28.635	39.025	9.906	1.00	13.80
B	C									
ATOM	1634	CG1	VAL	B	95	28.812	37.932	10.944	1.00	12.84
B	C									
ATOM	1635	CG2	VAL	B	95	27.246	39.611	9.997	1.00	11.25
B	C									
ATOM	1636	C	VAL	B	95	31.079	39.529	10.149	1.00	13.82
B	C									
ATOM	1637	O	VAL	B	95	31.690	39.410	11.211	1.00	13.76
B	O									
ATOM	1638	N	LEU	B	96	31.583	39.149	8.980	1.00	14.12
B	N									
ATOM	1639	CA	LEU	B	96	32.918	38.570	8.870	1.00	15.35
B	C									
ATOM	1640	CB	LEU	B	96	33.251	38.298	7.403	1.00	15.65
B	C									
ATOM	1641	CG	LEU	B	96	34.721	37.969	7.126	1.00	16.49
B	C									
ATOM	1642	CD1	LEU	B	96	35.100	36.677	7.833	1.00	13.79
B	C									
ATOM	1643	CD2	LEU	B	96	34.947	37.856	5.628	1.00	15.98
B	C									
ATOM	1644	C	LEU	B	96	34.010	39.471	9.465	1.00	16.84
B	C									
ATOM	1645	O	LEU	B	96	34.856	39.007	10.238	1.00	16.28
B	O									
ATOM	1646	N	ASN	B	97	33.994	40.752	9.097	1.00	15.44
B	N									
ATOM	1647	CA	ASN	B	97	34.997	41.699	9.590	1.00	16.09
B	C									
ATOM	1648	CB	ASN	B	97	34.901	43.021	8.821	1.00	17.20
B	C									
ATOM	1649	CG	ASN	B	97	35.362	42.873	7.385	1.00	18.71
B	C									

ATOM	1650	OD1	ASN	B	97	36.125	41.961	7.081	1.00	18.61
B	O									
ATOM	1651	ND2	ASN	B	97	34.910	43.761	6.499	1.00	17.57
B	N									
ATOM	1652	C	ASN	B	97	34.896	41.940	11.085	1.00	15.40
B	C									
ATOM	1653	O	ASN	B	97	35.914	42.005	11.777	1.00	16.22
B	O									
ATOM	1654	N	PHE	B	98	33.673	42.066	11.588	1.00	14.94
B	N									
ATOM	1655	CA	PHE	B	98	33.476	42.266	13.017	1.00	14.55
B	C									
ATOM	1656	CB	PHE	B	98	31.986	42.369	13.356	1.00	13.40
B	C									
ATOM	1657	CG	PHE	B	98	31.700	42.315	14.834	1.00	15.06
B	C									
ATOM	1658	CD1	PHE	B	98	31.958	43.415	15.649	1.00	14.98
B	C									
ATOM	1659	CD2	PHE	B	98	31.200	41.150	15.418	1.00	14.58
B	C									
ATOM	1660	CE1	PHE	B	98	31.720	43.360	17.032	1.00	14.56
B	C									
ATOM	1661	CE2	PHE	B	98	30.957	41.077	16.799	1.00	13.20
B	C									
ATOM	1662	CZ	PHE	B	98	31.218	42.188	17.608	1.00	12.63
B	C									
ATOM	1663	C	PHE	B	98	34.055	41.074	13.764	1.00	14.69
B	C									
ATOM	1664	O	PHE	B	98	34.793	41.227	14.735	1.00	14.16
B	O									
ATOM	1665	N	THR	B	99	33.705	39.880	13.300	1.00	14.39
B	N									
ATOM	1666	CA	THR	B	99	34.154	38.651	13.932	1.00	13.57
B	C									
ATOM	1667	CB	THR	B	99	33.490	37.433	13.257	1.00	12.94
B	C									
ATOM	1668	OG1	THR	B	99	32.059	37.576	13.316	1.00	12.53
B	O									
ATOM	1669	CG2	THR	B	99	33.896	36.143	13.958	1.00	12.70
B	C									
ATOM	1670	C	THR	B	99	35.677	38.516	13.893	1.00	13.81
B	C									
ATOM	1671	O	THR	B	99	36.295	38.142	14.884	1.00	12.81
B	O									
ATOM	1672	N	LEU	B	100	36.285	38.830	12.754	1.00	14.39
B	N									
ATOM	1673	CA	LEU	B	100	37.735	38.732	12.645	1.00	15.17
B	C									
ATOM	1674	CB	LEU	B	100	38.181	39.035	11.213	1.00	17.01
B	C									
ATOM	1675	CG	LEU	B	100	38.047	37.902	10.187	1.00	19.42
B	C									
ATOM	1676	CD1	LEU	B	100	38.195	38.470	8.778	1.00	20.62
B	C									
ATOM	1677	CD2	LEU	B	100	39.105	36.830	10.460	1.00	19.19
B	C									
ATOM	1678	C	LEU	B	100	38.439	39.694	13.608	1.00	16.32
B	C									



ATOM	1679	O	LEU B 100	39.276	39.289	14.412	1.00	15.91
B	O							
ATOM	1680	N	GLU B 101	38.079	40.968	13.533	1.00	15.77
B	N							
ATOM	1681	CA	GLU B 101	38.717	41.982	14.365	1.00	17.05
B	C							
ATOM	1682	CB	GLU B 101	38.439	43.370	13.781	1.00	20.26
B	C							
ATOM	1683	CG	GLU B 101	39.123	43.627	12.449	1.00	25.68
B	C							
ATOM	1684	CD	GLU B 101	38.898	45.038	11.941	1.00	29.94
B	C							
ATOM	1685	OE1	GLU B 101	39.087	45.992	12.730	1.00	31.04
B	O							
ATOM	1686	OE2	GLU B 101	38.541	45.192	10.752	1.00	31.88
B	O							
ATOM	1687	C	GLU B 101	38.366	41.992	15.846	1.00	15.48
B	C							
ATOM	1688	O	GLU B 101	39.232	42.214	16.684	1.00	14.15
B	O							
ATOM	1689	N	GLU B 102	37.103	41.749	16.169	1.00	14.59
B	N							
ATOM	1690	CA	GLU B 102	36.664	41.792	17.558	1.00	16.25
B	C							
ATOM	1691	CB	GLU B 102	35.292	42.462	17.624	1.00	15.08
B	C							
ATOM	1692	CG	GLU B 102	35.257	43.884	17.055	1.00	16.02
B	C							
ATOM	1693	CD	GLU B 102	35.992	44.893	17.928	1.00	15.88
B	C							
ATOM	1694	OE1	GLU B 102	35.953	44.745	19.168	1.00	15.08
B	O							
ATOM	1695	OE2	GLU B 102	36.595	45.846	17.383	1.00	15.59
B	O							
ATOM	1696	C	GLU B 102	36.611	40.451	18.283	1.00	17.63
B	C							
ATOM	1697	O	GLU B 102	36.475	40.408	19.510	1.00	16.52
B	O							
ATOM	1698	N	VAL B 103	36.721	39.357	17.539	1.00	16.71
B	N							
ATOM	1699	CA	VAL B 103	36.660	38.039	18.151	1.00	16.91
B	C							
ATOM	1700	CB	VAL B 103	35.392	37.286	17.709	1.00	16.05
B	C							
ATOM	1701	CG1	VAL B 103	35.394	35.881	18.310	1.00	19.19
B	C							
ATOM	1702	CG2	VAL B 103	34.157	38.054	18.144	1.00	18.67
B	C							
ATOM	1703	C	VAL B 103	37.845	37.128	17.862	1.00	17.70
B	C							
ATOM	1704	O	VAL B 103	38.540	36.680	18.784	1.00	16.69
B	O							
ATOM	1705	N	LEU B 104	38.067	36.855	16.581	1.00	16.37
B	N							
ATOM	1706	CA	LEU B 104	39.137	35.960	16.168	1.00	18.90
B	C							
ATOM	1707	CB	LEU B 104	38.984	35.614	14.687	1.00	15.60
B	C							

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ATOM	1708	CG	LEU B 104	37.636	34.955	14.362	1.00	16.30
B	C							
ATOM	1709	CD1	LEU B 104	37.541	34.663	12.874	1.00	14.16
B	C							
ATOM	1710	CD2	LEU B 104	37.485	33.671	15.162	1.00	16.44
B	C							
ATOM	1711	C	LEU B 104	40.539	36.471	16.447	1.00	20.44
B	C							
ATOM	1712	O	LEU B 104	41.326	35.780	17.086	1.00	20.16
B	O							
ATOM	1713	N	PHE B 105	40.870	37.666	15.979	1.00	21.99
B	N							
ATOM	1714	CA	PHE B 105	42.213	38.166	16.239	1.00	27.13
B	C							
ATOM	1715	CB	PHE B 105	42.387	39.579	15.675	1.00	28.81
B	C							
ATOM	1716	CG	PHE B 105	42.367	39.634	14.168	1.00	31.64
B	C							
ATOM	1717	CD1	PHE B 105	42.837	38.563	13.411	1.00	33.85
B	C							
ATOM	1718	CD2	PHE B 105	41.888	40.757	13.506	1.00	34.49
B	C							
ATOM	1719	CE1	PHE B 105	42.831	38.611	12.015	1.00	34.86
B	C							
ATOM	1720	CE2	PHE B 105	41.879	40.816	12.110	1.00	35.62
B	C							
ATOM	1721	CZ	PHE B 105	42.351	39.739	11.365	1.00	35.69
B	C							
ATOM	1722	C	PHE B 105	42.538	38.122	17.734	1.00	27.95
B	C							
ATOM	1723	O	PHE B 105	43.607	37.656	18.121	1.00	28.77
B	O							
ATOM	1724	N	PRO B 106	41.613	38.587	18.594	1.00	28.70
B	N							
ATOM	1725	CD	PRO B 106	40.390	39.341	18.266	1.00	28.83
B	C							
ATOM	1726	CA	PRO B 106	41.836	38.578	20.045	1.00	27.96
B	C							
ATOM	1727	CB	PRO B 106	40.590	39.280	20.589	1.00	28.83
B	C							
ATOM	1728	CG	PRO B 106	40.223	40.214	19.481	1.00	28.82
B	C							
ATOM	1729	C	PRO B 106	41.991	37.166	20.622	1.00	27.58
B	C							
ATOM	1730	O	PRO B 106	42.607	36.983	21.671	1.00	25.86
B	O							
ATOM	1731	N	GLN B 107	41.419	36.174	19.945	1.00	26.57
B	N							
ATOM	1732	CA	GLN B 107	41.499	34.784	20.394	1.00	27.34
B	C							
ATOM	1733	CB	GLN B 107	40.119	34.123	20.321	1.00	25.90
B	C							
ATOM	1734	CG	GLN B 107	39.027	34.737	21.181	1.00	27.05
B	C							
ATOM	1735	CD	GLN B 107	39.054	34.228	22.601	1.00	27.78
B	C							
ATOM	1736	OE1	GLN B 107	39.453	33.093	22.852	1.00	29.49
B	O							

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ATOM	1737	NE2	GLN	B	107	38.613	35.056	23.539	1.00	24.76
B	N									
ATOM	1738	C	GLN	B	107	42.457	33.994	19.497	1.00	28.04
B	C									
ATOM	1739	O	GLN	B	107	42.514	32.769	19.572	1.00	28.67
B	O									
ATOM	1740	N	SER	B	108	43.206	34.697	18.654	1.00	29.80
B	N									
ATOM	1741	CA	SER	B	108	44.125	34.059	17.710	1.00	31.32
B	C									
ATOM	1742	CB	SER	B	108	44.873	35.129	16.917	1.00	31.54
B	C									
ATOM	1743	OG	SER	B	108	45.612	35.971	17.784	1.00	33.99
B	O									
ATOM	1744	C	SER	B	108	45.131	33.064	18.291	1.00	32.91
B	C									
ATOM	1745	O	SER	B	108	45.661	32.220	17.562	1.00	32.09
B	O									
ATOM	1746	N	ASP	B	109	45.399	33.156	19.589	1.00	33.94
B	N									
ATOM	1747	CA	ASP	B	109	46.346	32.243	20.221	1.00	36.43
B	C									
ATOM	1748	CB	ASP	B	109	47.268	33.002	21.178	1.00	38.99
B	C									
ATOM	1749	CG	ASP	B	109	48.429	33.660	20.464	1.00	41.54
B	C									
ATOM	1750	OD1	ASP	B	109	48.195	34.463	19.536	1.00	43.90
B	O									
ATOM	1751	OD2	ASP	B	109	49.585	33.370	20.834	1.00	45.38
B	O									
ATOM	1752	C	ASP	B	109	45.669	31.103	20.965	1.00	35.97
B	C									
ATOM	1753	O	ASP	B	109	46.340	30.261	21.558	1.00	37.38
B	O									
ATOM	1754	N	ARG	B	110	44.342	31.070	20.929	1.00	34.07
B	N									
ATOM	1755	CA	ARG	B	110	43.595	30.019	21.606	1.00	32.11
B	C									
ATOM	1756	CB	ARG	B	110	42.483	30.628	22.457	1.00	34.24
B	C									
ATOM	1757	CG	ARG	B	110	42.974	31.587	23.523	1.00	38.78
B	C									
ATOM	1758	CD	ARG	B	110	41.799	32.210	24.253	1.00	42.57
B	C									
ATOM	1759	NE	ARG	B	110	42.213	33.153	25.285	1.00	46.77
B	N									
ATOM	1760	CZ	ARG	B	110	42.872	32.815	26.389	1.00	48.68
B	C									
ATOM	1761	NH1	ARG	B	110	43.198	31.545	26.610	1.00	48.55
B	N									
ATOM	1762	NH2	ARG	B	110	43.197	33.750	27.274	1.00	49.15
B	N									
ATOM	1763	C	ARG	B	110	42.989	29.047	20.601	1.00	29.74
B	C									
ATOM	1764	O	ARG	B	110	43.132	29.216	19.391	1.00	28.95
B	O									
ATOM	1765	N	PHE	B	111	42.314	28.025	21.119	1.00	28.23
B	N									

ATOM	1766	CA	PHE	B	111	41.671	27.018	20.289	1.00	25.68
B	C									
ATOM	1767	CB	PHE	B	111	40.429	27.619	19.627	1.00	25.02
B	C									
ATOM	1768	CG	PHE	B	111	39.351	28.002	20.604	1.00	21.00
B	C									
ATOM	1769	CD1	PHE	B	111	38.563	27.029	21.206	1.00	22.14
B	C									
ATOM	1770	CD2	PHE	B	111	39.151	29.331	20.954	1.00	21.84
B	C									
ATOM	1771	CE1	PHE	B	111	37.586	27.374	22.146	1.00	21.32
B	C									
ATOM	1772	CE2	PHE	B	111	38.178	29.687	21.891	1.00	22.27
B	C									
ATOM	1773	CZ	PHE	B	111	37.397	28.704	22.487	1.00	20.90
B	C									
ATOM	1774	C	PHE	B	111	42.610	26.436	19.239	1.00	25.72
B	C									
ATOM	1775	O	PHE	B	111	42.240	26.272	18.080	1.00	23.01
B	O									
ATOM	1776	N	GLN	B	112	43.829	26.119	19.659	1.00	26.79
B	N									
ATOM	1777	CA	GLN	B	112	44.820	25.530	18.764	1.00	28.39
B	C									
ATOM	1778	CB	GLN	B	112	46.211	25.622	19.392	1.00	29.98
B	C									
ATOM	1779	CG	GLN	B	112	46.709	27.043	19.587	1.00	33.82
B	C									
ATOM	1780	CD	GLN	B	112	48.085	27.100	20.227	1.00	36.64
B	C									
ATOM	1781	OE1	GLN	B	112	49.036	26.482	19.742	1.00	39.25
B	O									
ATOM	1782	NE2	GLN	B	112	48.199	27.847	21.320	1.00	36.49
B	N									
ATOM	1783	C	GLN	B	112	44.470	24.063	18.501	1.00	28.37
B	C									
ATOM	1784	O	GLN	B	112	43.903	23.389	19.358	1.00	27.65
B	O									
ATOM	1785	N	PRO	B	113	44.820	23.545	17.313	1.00	28.65
B	N									
ATOM	1786	CD	PRO	B	113	44.778	22.094	17.054	1.00	28.84
B	C									
ATOM	1787	CA	PRO	B	113	45.511	24.236	16.220	1.00	28.88
B	C									
ATOM	1788	CB	PRO	B	113	46.398	23.144	15.658	1.00	29.67
B	C									
ATOM	1789	CG	PRO	B	113	45.455	21.976	15.683	1.00	28.06
B	C									
ATOM	1790	C	PRO	B	113	44.550	24.757	15.160	1.00	29.20
B	C									
ATOM	1791	O	PRO	B	113	44.981	25.265	14.127	1.00	31.40
B	O									
ATOM	1792	N	TYR	B	114	43.253	24.624	15.414	1.00	29.48
B	N									
ATOM	1793	CA	TYR	B	114	42.232	25.047	14.459	1.00	29.46
B	C									
ATOM	1794	CB	TYR	B	114	40.839	24.695	14.992	1.00	30.23
B	C									

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ATOM	1795	CG	TYR	B	114	40.717	23.288	15.537	1.00	30.05
B	C									
ATOM	1796	CD1	TYR	B	114	40.943	22.177	14.724	1.00	32.21
B	C									
ATOM	1797	CE1	TYR	B	114	40.840	20.881	15.230	1.00	32.84
B	C									
ATOM	1798	CD2	TYR	B	114	40.383	23.069	16.871	1.00	31.34
B	C									
ATOM	1799	CE2	TYR	B	114	40.278	21.784	17.385	1.00	32.91
B	C									
ATOM	1800	CZ	TYR	B	114	40.508	20.695	16.562	1.00	33.51
B	C									
ATOM	1801	OH	TYR	B	114	40.413	19.424	17.081	1.00	35.76
B	O									
ATOM	1802	C	TYR	B	114	42.271	26.530	14.117	1.00	28.68
B	C									
ATOM	1803	O	TYR	B	114	42.347	26.909	12.948	1.00	29.12
B	O									
ATOM	1804	N	MET	B	115	42.213	27.366	15.146	1.00	28.56
B	N									
ATOM	1805	CA	MET	B	115	42.214	28.816	14.973	1.00	27.58
B	C									
ATOM	1806	CB	MET	B	115	42.343	29.488	16.344	1.00	27.94
B	C									
ATOM	1807	CG	MET	B	115	42.184	30.992	16.341	1.00	26.96
B	C									
ATOM	1808	SD	MET	B	115	40.483	31.474	16.055	1.00	27.58
B	S									
ATOM	1809	CE	MET	B	115	39.757	31.233	17.663	1.00	25.68
B	C									
ATOM	1810	C	MET	B	115	43.322	29.326	14.050	1.00	27.41
B	C									
ATOM	1811	O	MET	B	115	43.087	30.163	13.181	1.00	27.38
B	O									
ATOM	1812	N	GLN	B	116	44.530	28.814	14.240	1.00	28.20
B	N									
ATOM	1813	CA	GLN	B	116	45.679	29.243	13.458	1.00	29.73
B	C									
ATOM	1814	CB	GLN	B	116	46.935	28.565	13.997	1.00	31.41
B	C									
ATOM	1815	CG	GLN	B	116	47.200	28.852	15.474	1.00	34.08
B	C									
ATOM	1816	CD	GLN	B	116	46.074	28.388	16.390	1.00	35.14
B	C									
ATOM	1817	OE1	GLN	B	116	45.649	27.235	16.338	1.00	34.39
B	O									
ATOM	1818	NE2	GLN	B	116	45.590	29.292	17.239	1.00	37.03
B	N									
ATOM	1819	C	GLN	B	116	45.579	29.037	11.948	1.00	30.97
B	C									
ATOM	1820	O	GLN	B	116	46.279	29.697	11.184	1.00	31.99
B	O									
ATOM	1821	N	GLU	B	117	44.714	28.129	11.513	1.00	31.07
B	N									
ATOM	1822	CA	GLU	B	117	44.549	27.875	10.086	1.00	30.90
B	C									
ATOM	1823	CB	GLU	B	117	44.409	26.375	9.839	1.00	33.41
B	C									

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ATOM	1824	CG	GLU B 117	45.624	25.581	10.273	1.00	37.00
B	C							
ATOM	1825	CD	GLU B 117	45.416	24.089	10.155	1.00	39.15
B	C							
ATOM	1826	OE1	GLU B 117	44.547	23.549	10.877	1.00	41.69
B	O							
ATOM	1827	OE2	GLU B 117	46.123	23.460	9.339	1.00	40.83
B	O							
ATOM	1828	C	GLU B 117	43.328	28.601	9.532	1.00	28.96
B	C							
ATOM	1829	O	GLU B 117	43.359	29.151	8.428	1.00	29.54
B	O							
ATOM	1830	N	VAL B 118	42.256	28.613	10.314	1.00	25.88
B	N							
ATOM	1831	CA	VAL B 118	41.021	29.256	9.898	1.00	23.47
B	C							
ATOM	1832	CB	VAL B 118	39.869	28.897	10.868	1.00	23.29
B	C							
ATOM	1833	CG1	VAL B 118	38.603	29.663	10.491	1.00	21.92
B	C							
ATOM	1834	CG2	VAL B 118	39.618	27.391	10.829	1.00	22.44
B	C							
ATOM	1835	C	VAL B 118	41.115	30.773	9.772	1.00	22.53
B	C							
ATOM	1836	O	VAL B 118	40.622	31.347	8.804	1.00	21.65
B	O							
ATOM	1837	N	VAL B 119	41.748	31.429	10.739	1.00	23.10
B	N							
ATOM	1838	CA	VAL B 119	41.856	32.885	10.696	1.00	23.11
B	C							
ATOM	1839	CB	VAL B 119	42.573	33.432	11.941	1.00	23.48
B	C							
ATOM	1840	CG1	VAL B 119	42.727	34.937	11.830	1.00	24.03
B	C							
ATOM	1841	CG2	VAL B 119	41.771	33.094	13.182	1.00	25.07
B	C							
ATOM	1842	C	VAL B 119	42.537	33.427	9.438	1.00	22.58
B	C							
ATOM	1843	O	VAL B 119	42.025	34.350	8.805	1.00	21.65
B	O							
ATOM	1844	N	PRO B 120	43.705	32.874	9.063	1.00	23.16
B	N							
ATOM	1845	CD	PRO B 120	44.529	31.844	9.721	1.00	23.03
B	C							
ATOM	1846	CA	PRO B 120	44.371	33.378	7.856	1.00	22.66
B	C							
ATOM	1847	CB	PRO B 120	45.574	32.452	7.715	1.00	23.90
B	C							
ATOM	1848	CG	PRO B 120	45.899	32.114	9.133	1.00	23.90
B	C							
ATOM	1849	C	PRO B 120	43.434	33.294	6.654	1.00	23.50
B	C							
ATOM	1850	O	PRO B 120	43.346	34.226	5.846	1.00	21.52
B	O							
ATOM	1851	N	PHE B 121	42.727	32.169	6.555	1.00	23.36
B	N							
ATOM	1852	CA	PHE B 121	41.786	31.932	5.466	1.00	22.84
B	C							

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ATOM	1853	CB	PHE B 121	41.168	30.541	5.585	1.00	23.11
B	C							
ATOM	1854	CG	PHE B 121	40.089	30.278	4.579	1.00	24.84
B	C							
ATOM	1855	CD1	PHE B 121	40.400	30.074	3.241	1.00	25.82
B	C							
ATOM	1856	CD2	PHE B 121	38.755	30.260	4.966	1.00	25.84
B	C							
ATOM	1857	CE1	PHE B 121	39.396	29.856	2.302	1.00	25.59
B	C							
ATOM	1858	CE2	PHE B 121	37.744	30.043	4.033	1.00	27.74
B	C							
ATOM	1859	CZ	PHE B 121	38.067	29.841	2.699	1.00	26.97
B	C							
ATOM	1860	C	PHE B 121	40.679	32.974	5.474	1.00	22.35
B	C							
ATOM	1861	O	PHE B 121	40.382	33.572	4.443	1.00	22.39
B	O							
ATOM	1862	N	LEU B 122	40.059	33.180	6.633	1.00	22.63
B	N							
ATOM	1863	CA	LEU B 122	39.003	34.181	6.732	1.00	21.52
B	C							
ATOM	1864	CB	LEU B 122	38.321	34.102	8.109	1.00	20.83
B	C							
ATOM	1865	CG	LEU B 122	37.578	32.795	8.420	1.00	20.51
B	C							
ATOM	1866	CD1	LEU B 122	36.959	32.858	9.813	1.00	19.20
B	C							
ATOM	1867	CD2	LEU B 122	36.501	32.566	7.375	1.00	19.61
B	C							
ATOM	1868	C	LEU B 122	39.527	35.600	6.460	1.00	21.22
B	C							
ATOM	1869	O	LEU B 122	38.805	36.409	5.890	1.00	20.75
B	O							
ATOM	1870	N	ALA B 123	40.771	35.878	6.853	1.00	22.05
B	N							
ATOM	1871	CA	ALA B 123	41.379	37.190	6.637	1.00	24.52
B	C							
ATOM	1872	CB	ALA B 123	42.804	37.224	7.280	1.00	24.63
B	C							
ATOM	1873	C	ALA B 123	41.489	37.419	5.129	1.00	26.44
B	C							
ATOM	1874	O	ALA B 123	41.225	38.505	4.618	1.00	25.74
B	O							
ATOM	1875	N	ARG B 124	41.941	36.397	4.381	1.00	27.56
B	N							
ATOM	1876	CA	ARG B 124	42.092	36.492	2.915	1.00	28.25
B	C							
ATOM	1877	CB	AARG B 124	42.562	35.166	2.361	0.50	31.53
B	C							
ATOM	1878	CB	BARG B 124	42.543	35.160	2.316	0.50	31.52
B	C							
ATOM	1879	CG	AARG B 124	43.971	34.730	2.819	0.50	34.27
B	C							
ATOM	1880	CG	BARG B 124	43.953	34.764	2.660	0.50	34.62
B	C							
ATOM	1881	CD	AARG B 124	44.500	33.566	1.961	0.50	36.72
B	C							

ATOM	1882	CD	BARG	B	124	44.485	33.793	1.624	0.50	36.96
B	C									
ATOM	1883	NE	AARG	B	124	44.367	32.250	2.587	0.50	38.21
B	N									
ATOM	1884	NE	BARG	B	124	43.633	32.620	1.416	0.50	39.16
B	N									
ATOM	1885	CZ	AARG	B	124	45.302	31.685	3.346	0.50	39.41
B	C									
ATOM	1886	CZ	BARG	B	124	42.571	32.573	0.613	0.50	39.85
B	C									
ATOM	1887	NH1AARG		B	124	46.444	32.318	3.574	0.50	39.45
B	N									
ATOM	1888	NH1BARG		B	124	42.196	33.638	-0.084	0.50	39.88
B	N									
ATOM	1889	NH2AARG		B	124	45.097	30.487	3.874	0.50	40.70
B	N									
ATOM	1890	NH2BARG		B	124	41.878	31.449	0.504	0.50	40.63
B	N									
ATOM	1891	C	ARG	B	124	40.755	36.861	2.270	1.00	28.59
B	C									
ATOM	1892	O	ARG	B	124	40.699	37.698	1.347	1.00	28.10
B	O									
ATOM	1893	N	LEU	B	125	39.685	36.193	2.734	1.00	28.01
B	N									
ATOM	1894	CA	LEU	B	125	38.367	36.466	2.203	1.00	25.98
B	C									
ATOM	1895	CB	LEU	B	125	37.333	35.525	2.822	1.00	27.46
B	C									
ATOM	1896	CG	LEU	B	125	37.385	34.019	2.530	1.00	27.82
B	C									
ATOM	1897	CD1	LEU	B	125	36.107	33.354	3.052	1.00	26.92
B	C									
ATOM	1898	CD2	LEU	B	125	37.519	33.771	1.039	1.00	27.76
B	C									
ATOM	1899	C	LEU	B	125	37.940	37.905	2.469	1.00	25.43
B	C									
ATOM	1900	O	LEU	B	125	37.301	38.547	1.629	1.00	25.94
B	O									
ATOM	1901	N	SER	B	126	38.262	38.392	3.660	1.00	24.59
B	N									
ATOM	1902	CA	SER	B	126	37.937	39.757	4.040	1.00	25.45
B	C									
ATOM	1903	CB	SER	B	126	38.427	40.030	5.463	1.00	25.70
B	C									
ATOM	1904	OG	SER	B	126	38.216	41.382	5.819	1.00	24.65
B	O									
ATOM	1905	C	SER	B	126	38.671	40.668	3.067	1.00	26.58
B	C									
ATOM	1906	O	SER	B	126	38.126	41.664	2.584	1.00	25.56
B	O									
ATOM	1907	N	ASN	B	127	39.920	40.311	2.789	1.00	28.53
B	N									
ATOM	1908	CA	ASN	B	127	40.766	41.069	1.875	1.00	31.42
B	C									
ATOM	1909	CB	ASN	B	127	42.149	40.415	1.810	1.00	33.56
B	C									
ATOM	1910	CG	ASN	B	127	43.145	41.230	1.017	1.00	37.76
B	C									



ATOM	1911	OD1	ASN	B	127	43.392	42.396	1.326	1.00	41.52
B	O									
ATOM	1912	ND2	ASN	B	127	43.734	40.617	-0.008	1.00	37.74
B	N									
ATOM	1913	C	ASN	B	127	40.114	41.110	0.492	1.00	31.83
B	C									
ATOM	1914	O	ASN	B	127	40.081	42.154	-0.160	1.00	32.67
B	O									
ATOM	1915	N	ARG	B	128	39.584	39.971	0.057	1.00	33.16
B	N									
ATOM	1916	CA	ARG	B	128	38.919	39.872	-1.239	1.00	35.03
B	C									
ATOM	1917	CB	ARG	B	128	38.477	38.429	-1.499	1.00	37.42
B	C									
ATOM	1918	CG	ARG	B	128	39.572	37.384	-1.393	1.00	40.66
B	C									
ATOM	1919	CD	ARG	B	128	40.484	37.388	-2.602	1.00	44.62
B	C									
ATOM	1920	NE	ARG	B	128	41.399	36.248	-2.596	1.00	47.25
B	N									
ATOM	1921	CZ	ARG	B	128	42.370	36.069	-1.706	1.00	49.09
B	C									
ATOM	1922	NH1	ARG	B	128	42.562	36.957	-0.737	1.00	49.49
B	N									
ATOM	1923	NH2	ARG	B	128	43.155	35.002	-1.787	1.00	49.90
B	N									
ATOM	1924	C	ARG	B	128	37.686	40.780	-1.311	1.00	35.69
B	C									
ATOM	1925	O	ARG	B	128	37.401	41.370	-2.352	1.00	35.80
B	O									
ATOM	1926	N	LEU	B	129	36.955	40.886	-0.206	1.00	35.75
B	N									
ATOM	1927	CA	LEU	B	129	35.746	41.709	-0.161	1.00	36.71
B	C									
ATOM	1928	CB	LEU	B	129	34.816	41.213	0.952	1.00	35.61
B	C									
ATOM	1929	CG	LEU	B	129	34.227	39.810	0.784	1.00	36.13
B	C									
ATOM	1930	CD1	LEU	B	129	33.424	39.445	2.017	1.00	35.68
B	C									
ATOM	1931	CD2	LEU	B	129	33.344	39.761	-0.454	1.00	34.32
B	C									
ATOM	1932	C	LEU	B	129	36.018	43.200	0.043	1.00	37.24
B	C									
ATOM	1933	O	LEU	B	129	35.086	43.989	0.178	1.00	37.30
B	O									
ATOM	1934	N	SER	B	130	37.291	43.577	0.059	1.00	39.20
B	N									
ATOM	1935	CA	SER	B	130	37.693	44.969	0.268	1.00	41.51
B	C									
ATOM	1936	CB	SER	B	130	39.122	45.191	-0.238	1.00	41.64
B	C									
ATOM	1937	OG	SER	B	130	40.062	44.614	0.651	1.00	44.96
B	O									
ATOM	1938	C	SER	B	130	36.789	46.030	-0.345	1.00	41.71
B	C									
ATOM	1939	O	SER	B	130	36.579	46.056	-1.550	1.00	43.01
B	O									

ATOM	1940	N	THR B 131	36.259	46.900	0.508	1.00	42.65
B	N							
ATOM	1941	CA	THR B 131	35.399	48.012	0.103	1.00	43.65
B	C							
ATOM	1942	CB	THR B 131	36.223	49.110	-0.617	1.00	44.32
B	C							
ATOM	1943	OG1	THR B 131	36.682	48.620	-1.885	1.00	45.77
B	O							
ATOM	1944	CG2	THR B 131	37.428	49.511	0.236	1.00	44.02
B	C							
ATOM	1945	C	THR B 131	34.161	47.723	-0.747	1.00	43.82
B	C							
ATOM	1946	O	THR B 131	33.401	48.649	-1.041	1.00	43.74
B	O							
ATOM	1947	N	CYS B 132	33.945	46.470	-1.146	1.00	43.43
B	N							
ATOM	1948	CA	CYS B 132	32.762	46.157	-1.949	1.00	42.56
B	C							
ATOM	1949	C	CYS B 132	31.564	46.639	-1.146	1.00	42.53
B	C							
ATOM	1950	O	CYS B 132	31.515	46.452	0.068	1.00	42.41
B	O							
ATOM	1951	CB	CYS B 132	32.644	44.651	-2.205	1.00	41.08
B	C							
ATOM	1952	SG	CYS B 132	32.191	43.674	-0.738	1.00	40.07
B	S							
ATOM	1953	N	HIS B 133	30.608	47.277	-1.813	1.00	44.03
B	N							
ATOM	1954	CA	HIS B 133	29.434	47.790	-1.120	1.00	45.92
B	C							
ATOM	1955	CB	HIS B 133	29.661	49.247	-0.723	1.00	48.01
B	C							
ATOM	1956	CG	HIS B 133	29.999	50.136	-1.877	1.00	50.95
B	C							
ATOM	1957	CD2	HIS B 133	29.344	51.195	-2.408	1.00	51.52
B	C							
ATOM	1958	ND1	HIS B 133	31.132	49.961	-2.642	1.00	52.14
B	N							
ATOM	1959	CE1	HIS B 133	31.161	50.875	-3.596	1.00	52.81
B	C							
ATOM	1960	NE2	HIS B 133	30.088	51.636	-3.477	1.00	52.91
B	N							
ATOM	1961	C	HIS B 133	28.158	47.680	-1.940	1.00	45.88
B	C							
ATOM	1962	O	HIS B 133	28.143	47.067	-3.005	1.00	45.95
B	O							
ATOM	1963	N	ILE B 134	27.086	48.281	-1.433	1.00	46.79
B	N							
ATOM	1964	CA	ILE B 134	25.798	48.245	-2.110	1.00	48.22
B	C							
ATOM	1965	CB	ILE B 134	24.686	47.725	-1.172	1.00	47.47
B	C							
ATOM	1966	CG2	ILE B 134	25.035	46.328	-0.684	1.00	47.42
B	C							
ATOM	1967	CG1	ILE B 134	24.515	48.672	0.016	1.00	46.57
B	C							
ATOM	1968	CD	ILE B 134	23.426	48.248	0.977	1.00	47.17
B	C							

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ATOM	1969	C	ILE B 134	25.385	49.614	-2.644	1.00	49.84
B	C							
ATOM	1970	O	ILE B 134	26.079	50.611	-2.439	1.00	49.80
B	O							
ATOM	1971	N	GLU B 135	24.243	49.642	-3.326	1.00	50.44
B	N							
ATOM	1972	CA	GLU B 135	23.700	50.860	-3.921	1.00	51.87
B	C							
ATOM	1973	CB	GLU B 135	22.405	50.531	-4.671	1.00	53.19
B	C							
ATOM	1974	CG	GLU B 135	22.597	49.598	-5.859	1.00	55.61
B	C							
ATOM	1975	CD	GLU B 135	23.283	48.298	-5.475	1.00	57.90
B	C							
ATOM	1976	OE1	GLU B 135	22.787	47.613	-4.554	1.00	58.58
B	O							
ATOM	1977	OE2	GLU B 135	24.317	47.963	-6.093	1.00	59.79
B	O							
ATOM	1978	C	GLU B 135	23.445	51.989	-2.918	1.00	51.36
B	C							
ATOM	1979	O	GLU B 135	24.324	52.820	-2.677	1.00	51.02
B	O							
ATOM	1980	N	GLY B 136	22.245	52.022	-2.341	1.00	50.44
B	N							
ATOM	1981	CA	GLY B 136	21.930	53.074	-1.393	1.00	49.30
B	C							
ATOM	1982	C	GLY B 136	21.197	52.672	-0.128	1.00	47.53
B	C							
ATOM	1983	O	GLY B 136	20.289	51.839	-0.147	1.00	46.93
B	O							
ATOM	1984	N	ASP B 137	21.614	53.284	0.976	1.00	46.58
B	N							
ATOM	1985	CA	ASP B 137	21.027	53.064	2.293	1.00	45.28
B	C							
ATOM	1986	CB	ASP B 137	19.559	53.486	2.277	1.00	47.28
B	C							
ATOM	1987	CG	ASP B 137	18.981	53.623	3.661	1.00	48.41
B	C							
ATOM	1988	OD1	ASP B 137	19.131	52.681	4.465	1.00	48.28
B	O							
ATOM	1989	OD2	ASP B 137	18.378	54.675	3.947	1.00	51.40
B	O							
ATOM	1990	C	ASP B 137	21.133	51.650	2.844	1.00	43.55
B	C							
ATOM	1991	O	ASP B 137	20.277	50.803	2.590	1.00	43.30
B	O							
ATOM	1992	N	ASP B 138	22.184	51.416	3.620	1.00	40.92
B	N							
ATOM	1993	CA	ASP B 138	22.419	50.118	4.237	1.00	38.17
B	C							
ATOM	1994	CB	ASP B 138	23.899	49.774	4.155	1.00	37.09
B	C							
ATOM	1995	CG	ASP B 138	24.751	50.703	4.992	1.00	38.19
B	C							
ATOM	1996	OD1	ASP B 138	24.292	51.828	5.283	1.00	38.67
B	O							
ATOM	1997	OD2	ASP B 138	25.882	50.319	5.354	1.00	39.46
B	O							

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ATOM	1998	C	ASP B 138	21.988	50.124	5.712	1.00	36.48
B	C							
ATOM	1999	O	ASP B 138	22.428	49.286	6.501	1.00	36.23
B	O							
ATOM	2000	N	LEU B 139	21.124	51.065	6.076	1.00	35.08
B	N							
ATOM	2001	CA	LEU B 139	20.650	51.196	7.450	1.00	33.13
B	C							
ATOM	2002	CB	LEU B 139	19.592	52.298	7.533	1.00	36.06
B	C							
ATOM	2003	CG	LEU B 139	19.099	52.661	8.934	1.00	37.59
B	C							
ATOM	2004	CD1	LEU B 139	20.224	53.321	9.706	1.00	39.27
B	C							
ATOM	2005	CD2	LEU B 139	17.909	53.599	8.840	1.00	40.35
B	C							
ATOM	2006	C	LEU B 139	20.087	49.903	8.030	1.00	31.75
B	C							
ATOM	2007	O	LEU B 139	20.423	49.524	9.153	1.00	31.56
B	O							
ATOM	2008	N	HIS B 140	19.227	49.226	7.275	1.00	29.29
B	N							
ATOM	2009	CA	HIS B 140	18.634	47.975	7.748	1.00	27.87
B	C							
ATOM	2010	CB	HIS B 140	17.598	47.465	6.738	1.00	29.34
B	C							
ATOM	2011	CG	HIS B 140	18.158	47.209	5.374	1.00	30.92
B	C							
ATOM	2012	CD2	HIS B 140	18.179	46.088	4.614	1.00	32.52
B	C							
ATOM	2013	ND1	HIS B 140	18.796	48.183	4.636	1.00	33.09
B	N							
ATOM	2014	CE1	HIS B 140	19.187	47.672	3.481	1.00	33.64
B	C							
ATOM	2015	NE2	HIS B 140	18.826	46.403	3.442	1.00	33.59
B	N							
ATOM	2016	C	HIS B 140	19.714	46.912	7.977	1.00	24.95
B	C							
ATOM	2017	O	HIS B 140	19.614	46.083	8.878	1.00	24.47
B	O							
ATOM	2018	N	ILE B 141	20.752	46.946	7.156	1.00	23.58
B	N							
ATOM	2019	CA	ILE B 141	21.840	45.991	7.289	1.00	22.50
B	C							
ATOM	2020	CB	ILE B 141	22.765	46.043	6.059	1.00	23.20
B	C							
ATOM	2021	CG2	ILE B 141	23.982	45.171	6.283	1.00	22.62
B	C							
ATOM	2022	CG1	ILE B 141	21.983	45.592	4.818	1.00	24.14
B	C							
ATOM	2023	CD	ILE B 141	22.783	45.609	3.541	1.00	26.45
B	C							
ATOM	2024	C	ILE B 141	22.641	46.287	8.556	1.00	22.44
B	C							
ATOM	2025	O	ILE B 141	22.899	45.390	9.361	1.00	19.54
B	O							
ATOM	2026	N	GLN B 142	23.020	47.548	8.738	1.00	21.44
B	N							

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ATOM	2027	CA	GLN B 142	23.792	47.932	9.913	1.00	20.93
B	C							
ATOM	2028	CB	GLN B 142	24.152	49.418	9.858	1.00	23.51
B	C							
ATOM	2029	CG	GLN B 142	25.108	49.807	8.734	1.00	27.67
B	C							
ATOM	2030	CD	GLN B 142	26.345	48.920	8.666	1.00	31.25
B	C							
ATOM	2031	OE1	GLN B 142	26.874	48.488	9.692	1.00	33.98
B	O							
ATOM	2032	NE2	GLN B 142	26.819	48.659	7.451	1.00	31.45
B	N							
ATOM	2033	C	GLN B 142	23.031	47.634	11.202	1.00	19.58
B	C							
ATOM	2034	O	GLN B 142	23.621	47.216	12.195	1.00	19.52
B	O							
ATOM	2035	N	ARG B 143	21.718	47.847	11.182	1.00	19.46
B	N							
ATOM	2036	CA	ARG B 143	20.891	47.598	12.355	1.00	18.97
B	C							
ATOM	2037	CB	ARG B 143	19.454	48.084	12.117	1.00	19.80
B	C							
ATOM	2038	CG	ARG B 143	18.572	47.982	13.361	1.00	20.29
B	C							
ATOM	2039	CD	ARG B 143	17.151	48.457	13.118	1.00	24.78
B	C							
ATOM	2040	NE	ARG B 143	17.081	49.859	12.703	1.00	27.22
B	N							
ATOM	2041	CZ	ARG B 143	16.831	50.261	11.459	1.00	29.43
B	C							
ATOM	2042	NH1	ARG B 143	16.625	49.367	10.499	1.00	28.10
B	N							
ATOM	2043	NH2	ARG B 143	16.785	51.557	11.172	1.00	29.11
B	N							
ATOM	2044	C	ARG B 143	20.879	46.116	12.716	1.00	19.02
B	C							
ATOM	2045	O	ARG B 143	20.936	45.751	13.896	1.00	18.36
B	O							
ATOM	2046	N	ASN B 144	20.795	45.259	11.703	1.00	17.05
B	N							
ATOM	2047	CA	ASN B 144	20.783	43.822	11.944	1.00	17.50
B	C							
ATOM	2048	CB	ASN B 144	20.492	43.053	10.649	1.00	16.62
B	C							
ATOM	2049	CG	ASN B 144	19.062	43.240	10.169	1.00	18.56
B	C							
ATOM	2050	OD1	ASN B 144	18.280	43.963	10.781	1.00	15.87
B	O							
ATOM	2051	ND2	ASN B 144	18.714	42.582	9.070	1.00	18.04
B	N							
ATOM	2052	C	ASN B 144	22.125	43.381	12.503	1.00	16.92
B	C							
ATOM	2053	O	ASN B 144	22.181	42.547	13.400	1.00	16.92
B	O							
ATOM	2054	N	VAL B 145	23.205	43.943	11.967	1.00	15.33
B	N							
ATOM	2055	CA	VAL B 145	24.544	43.598	12.423	1.00	15.98
B	C							

ATOM	2056	CB	VAL	B	145	25.615	44.191	11.469	1.00	17.14
B	C									
ATOM	2057	CG1	VAL	B	145	27.020	43.920	12.007	1.00	17.91
B	C									
ATOM	2058	CG2	VAL	B	145	25.456	43.584	10.080	1.00	18.98
B	C									
ATOM	2059	C	VAL	B	145	24.760	44.118	13.846	1.00	16.15
B	C									
ATOM	2060	O	VAL	B	145	25.396	43.454	14.672	1.00	13.69
B	O									
ATOM	2061	N	GLN	B	146	24.221	45.302	14.134	1.00	14.53
B	N									
ATOM	2062	CA	GLN	B	146	24.359	45.893	15.464	1.00	12.59
B	C									
ATOM	2063	CB	GLN	B	146	23.598	47.222	15.546	1.00	12.98
B	C									
ATOM	2064	CG	GLN	B	146	23.739	47.970	16.885	1.00	15.51
B	C									
ATOM	2065	CD	GLN	B	146	25.100	48.641	17.058	1.00	18.34
B	C									
ATOM	2066	OE1	GLN	B	146	25.593	49.306	16.148	1.00	17.29
B	O									
ATOM	2067	NE2	GLN	B	146	25.700	48.483	18.233	1.00	19.22
B	N									
ATOM	2068	C	GLN	B	146	23.814	44.926	16.516	1.00	13.75
B	C									
ATOM	2069	O	GLN	B	146	24.388	44.778	17.592	1.00	11.09
B	O									
ATOM	2070	N	LYS	B	147	22.703	44.267	16.205	1.00	14.74
B	N									
ATOM	2071	CA	LYS	B	147	22.112	43.326	17.147	1.00	15.33
B	C									
ATOM	2072	CB	LYS	B	147	20.820	42.737	16.575	1.00	19.41
B	C									
ATOM	2073	CG	LYS	B	147	19.632	43.681	16.657	1.00	24.48
B	C									
ATOM	2074	CD	LYS	B	147	18.351	43.003	16.173	1.00	27.59
B	C									
ATOM	2075	CE	LYS	B	147	17.113	43.791	16.583	1.00	30.10
B	C									
ATOM	2076	NZ	LYS	B	147	17.197	45.226	16.199	1.00	32.34
B	N									
ATOM	2077	C	LYS	B	147	23.075	42.202	17.488	1.00	14.99
B	C									
ATOM	2078	O	LYS	B	147	23.242	41.851	18.656	1.00	13.88
B	O									
ATOM	2079	N	LEU	B	148	23.698	41.630	16.463	1.00	13.47
B	N									
ATOM	2080	CA	LEU	B	148	24.646	40.546	16.664	1.00	11.96
B	C									
ATOM	2081	CB	LEU	B	148	25.128	40.020	15.309	1.00	11.28
B	C									
ATOM	2082	CG	LEU	B	148	26.174	38.901	15.273	1.00	13.54
B	C									
ATOM	2083	CD1	LEU	B	148	26.101	38.200	13.936	1.00	12.19
B	C									
ATOM	2084	CD2	LEU	B	148	27.561	39.466	15.516	1.00	12.71
B	C									

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ATOM	2085	C	LEU B 148	25.818	41.072	17.486	1.00	12.75
B	C							
ATOM	2086	O	LEU B 148	26.256	40.428	18.434	1.00	13.22
B	O							
ATOM	2087	N	LYS B 149	26.309	42.254	17.121	1.00	12.62
B	N							
ATOM	2088	CA	LYS B 149	27.423	42.886	17.818	1.00	13.95
B	C							
ATOM	2089	CB	LYS B 149	27.794	44.203	17.124	1.00	13.88
B	C							
ATOM	2090	CG	LYS B 149	28.555	43.999	15.828	1.00	17.34
B	C							
ATOM	2091	CD	LYS B 149	28.430	45.170	14.872	1.00	22.47
B	C							
ATOM	2092	CE	LYS B 149	28.881	46.482	15.472	1.00	25.42
B	C							
ATOM	2093	NZ	LYS B 149	29.064	47.513	14.402	1.00	24.53
B	N							
ATOM	2094	C	LYS B 149	27.122	43.137	19.293	1.00	14.22
B	C							
ATOM	2095	O	LYS B 149	27.956	42.850	20.151	1.00	15.40
B	O							
ATOM	2096	N	ASP B 150	25.939	43.663	19.593	1.00	13.64
B	N							
ATOM	2097	CA	ASP B 150	25.576	43.928	20.988	1.00	13.95
B	C							
ATOM	2098	CB	ASP B 150	24.198	44.589	21.080	1.00	15.50
B	C							
ATOM	2099	CG	ASP B 150	24.172	45.985	20.493	1.00	16.66
B	C							
ATOM	2100	OD1	ASP B 150	25.253	46.586	20.324	1.00	16.66
B	O							
ATOM	2101	OD2	ASP B 150	23.055	46.480	20.212	1.00	19.61
B	O							
ATOM	2102	C	ASP B 150	25.554	42.661	21.843	1.00	13.62
B	C							
ATOM	2103	O	ASP B 150	25.986	42.655	23.002	1.00	12.88
B	O							
ATOM	2104	N	THR B 151	25.017	41.591	21.276	1.00	12.91
B	N							
ATOM	2105	CA	THR B 151	24.926	40.326	21.988	1.00	14.27
B	C							
ATOM	2106	CB	THR B 151	24.211	39.278	21.127	1.00	16.02
B	C							
ATOM	2107	OG1	THR B 151	22.904	39.763	20.802	1.00	15.49
B	O							
ATOM	2108	CG2	THR B 151	24.101	37.951	21.862	1.00	15.10
B	C							
ATOM	2109	C	THR B 151	26.313	39.830	22.340	1.00	14.06
B	C							
ATOM	2110	O	THR B 151	26.554	39.381	23.460	1.00	15.38
B	O							
ATOM	2111	N	VAL B 152	27.231	39.915	21.383	1.00	12.61
B	N							
ATOM	2112	CA	VAL B 152	28.594	39.469	21.621	1.00	13.27
B	C							
ATOM	2113	CB	VAL B 152	29.429	39.499	20.321	1.00	13.23
B	C							

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ATOM	2114	CG1	VAL	B	152	30.900	39.371	20.647	1.00	12.74
B	C									
ATOM	2115	CG2	VAL	B	152	29.001	38.354	19.409	1.00	13.59
B	C									
ATOM	2116	C	VAL	B	152	29.283	40.335	22.672	1.00	12.43
B	C									
ATOM	2117	O	VAL	B	152	29.916	39.817	23.587	1.00	13.68
B	O									
ATOM	2118	N	LYS	B	153	29.141	41.653	22.549	1.00	11.31
B	N									
ATOM	2119	CA	LYS	B	153	29.786	42.570	23.489	1.00	9.49
B	C									
ATOM	2120	CB	LYS	B	153	29.720	44.011	22.965	1.00	9.07
B	C									
ATOM	2121	CG	LYS	B	153	30.559	44.253	21.708	1.00	7.62
B	C									
ATOM	2122	CD	LYS	B	153	32.027	43.864	21.936	1.00	9.41
B	C									
ATOM	2123	CE	LYS	B	153	32.891	44.041	20.688	1.00	9.65
B	C									
ATOM	2124	NZ	LYS	B	153	34.308	43.621	20.957	1.00	8.41
B	N									
ATOM	2125	C	LYS	B	153	29.231	42.505	24.902	1.00	9.60
B	C									
ATOM	2126	O	LYS	B	153	29.990	42.550	25.872	1.00	10.58
B	O									
ATOM	2127	N	LYS	B	154	27.917	42.398	25.034	1.00	10.82
B	N									
ATOM	2128	CA	LYS	B	154	27.318	42.330	26.362	1.00	12.31
B	C									
ATOM	2129	CB	LYS	B	154	25.787	42.296	26.255	1.00	14.53
B	C									
ATOM	2130	CG	LYS	B	154	25.109	41.913	27.561	1.00	20.06
B	C									
ATOM	2131	CD	LYS	B	154	23.589	42.030	27.501	1.00	24.39
B	C									
ATOM	2132	CE	LYS	B	154	22.991	41.812	28.891	1.00	24.64
B	C									
ATOM	2133	NZ	LYS	B	154	21.499	41.697	28.874	1.00	27.27
B	N									
ATOM	2134	C	LYS	B	154	27.808	41.105	27.138	1.00	14.73
B	C									
ATOM	2135	O	LYS	B	154	27.940	41.141	28.366	1.00	13.45
B	O									
ATOM	2136	N	LEU	B	155	28.090	40.026	26.412	1.00	14.59
B	N									
ATOM	2137	CA	LEU	B	155	28.546	38.783	27.024	1.00	15.48
B	C									
ATOM	2138	CB	LEU	B	155	28.120	37.596	26.156	1.00	14.97
B	C									
ATOM	2139	CG	LEU	B	155	26.614	37.319	26.219	1.00	16.78
B	C									
ATOM	2140	CD1	LEU	B	155	26.251	36.184	25.283	1.00	17.88
B	C									
ATOM	2141	CD2	LEU	B	155	26.233	36.976	27.659	1.00	18.88
B	C									
ATOM	2142	C	LEU	B	155	30.043	38.710	27.305	1.00	16.52
B	C									



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ATOM	2143	O	LEU B 155	30.522	37.749	27.904	1.00	16.70
B	O							
ATOM	2144	N	GLY B 156	30.788	39.723	26.878	1.00	16.38
B	N							
ATOM	2145	CA	GLY B 156	32.213	39.716	27.146	1.00	17.98
B	C							
ATOM	2146	C	GLY B 156	32.918	38.521	26.542	1.00	18.96
B	C							
ATOM	2147	O	GLY B 156	32.658	38.159	25.398	1.00	19.62
B	O							
ATOM	2148	N	GLU B 157	33.807	37.897	27.305	1.00	20.01
B	N							
ATOM	2149	CA	GLU B 157	34.547	36.751	26.790	1.00	22.65
B	C							
ATOM	2150	CB	GLU B 157	35.504	36.198	27.844	1.00	26.57
B	C							
ATOM	2151	CG	GLU B 157	36.377	35.060	27.323	1.00	32.56
B	C							
ATOM	2152	CD	GLU B 157	37.622	34.860	28.160	1.00	36.42
B	C							
ATOM	2153	OE1	GLU B 157	37.487	34.500	29.348	1.00	39.12
B	O							
ATOM	2154	OE2	GLU B 157	38.738	35.071	27.632	1.00	40.09
B	O							
ATOM	2155	C	GLU B 157	33.642	35.628	26.304	1.00	21.05
B	C							
ATOM	2156	O	GLU B 157	33.940	34.972	25.309	1.00	19.94
B	O							
ATOM	2157	N	SER B 158	32.551	35.395	27.025	1.00	20.79
B	N							
ATOM	2158	CA	SER B 158	31.602	34.357	26.650	1.00	20.47
B	C							
ATOM	2159	CB	SER B 158	30.481	34.264	27.684	1.00	21.91
B	C							
ATOM	2160	OG	SER B 158	31.000	33.902	28.948	1.00	26.50
B	O							
ATOM	2161	C	SER B 158	31.006	34.696	25.291	1.00	19.88
B	C							
ATOM	2162	O	SER B 158	30.649	33.803	24.519	1.00	20.24
B	O							
ATOM	2163	N	GLY B 159	30.890	35.991	25.010	1.00	18.62
B	N							
ATOM	2164	CA	GLY B 159	30.343	36.426	23.733	1.00	17.19
B	C							
ATOM	2165	C	GLY B 159	31.272	36.008	22.611	1.00	15.21
B	C							
ATOM	2166	O	GLY B 159	30.828	35.574	21.536	1.00	13.42
B	O							
ATOM	2167	N	GLU B 160	32.569	36.138	22.862	1.00	12.99
B	N							
ATOM	2168	CA	GLU B 160	33.571	35.759	21.880	1.00	15.94
B	C							
ATOM	2169	CB	GLU B 160	34.963	36.197	22.349	1.00	18.02
B	C							
ATOM	2170	CG	GLU B 160	35.143	37.708	22.329	1.00	21.23
B	C							
ATOM	2171	CD	GLU B 160	36.471	38.151	22.913	1.00	25.05
B	C							

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ATOM	2172	OE1	GLU	B	160	37.519	37.597	22.522	1.00	26.71
B	O									
ATOM	2173	OE2	GLU	B	160	36.467	39.065	23.758	1.00	26.22
B	O									
ATOM	2174	C	GLU	B	160	33.533	34.252	21.646	1.00	16.05
B	C									
ATOM	2175	O	GLU	B	160	33.584	33.791	20.503	1.00	16.68
B	O									
ATOM	2176	N	ILE	B	161	33.430	33.489	22.728	1.00	15.72
B	N									
ATOM	2177	CA	ILE	B	161	33.380	32.033	22.628	1.00	15.75
B	C									
ATOM	2178	CB	AILE	B	161	33.334	31.371	24.025	0.50	17.43
B	C									
ATOM	2179	CB	BILE	B	161	33.345	31.389	24.043	0.50	17.65
B	C									
ATOM	2180	CG2AILE	B	161	33.225	29.860	23.887	0.50	18.33	
B	C									
ATOM	2181	CG2BILE	B	161	33.204	29.879	23.924	0.50	18.35	
B	C									
ATOM	2182	CG1AILE	B	161	34.588	31.753	24.820	0.50	18.68	
B	C									
ATOM	2183	CG1BILE	B	161	34.627	31.750	24.803	0.50	18.95	
B	C									
ATOM	2184	CD	AILE	B	161	35.890	31.386	24.139	0.50	18.08
B	C									
ATOM	2185	CD	BILE	B	161	34.640	31.314	26.252	0.50	19.38
B	C									
ATOM	2186	C	ILE	B	161	32.151	31.616	21.828	1.00	15.04
B	C									
ATOM	2187	O	ILE	B	161	32.233	30.745	20.960	1.00	13.38
B	O									
ATOM	2188	N	LYS	B	162	31.017	32.251	22.110	1.00	14.57
B	N									
ATOM	2189	CA	LYS	B	162	29.782	31.938	21.401	1.00	14.05
B	C									
ATOM	2190	CB	LYS	B	162	28.621	32.771	21.954	1.00	14.23
B	C									
ATOM	2191	CG	LYS	B	162	27.299	32.559	21.206	1.00	15.87
B	C									
ATOM	2192	CD	LYS	B	162	26.211	33.520	21.678	1.00	16.15
B	C									
ATOM	2193	CE	LYS	B	162	25.913	33.359	23.163	1.00	18.43
B	C									
ATOM	2194	NZ	LYS	B	162	25.341	32.018	23.490	1.00	22.02
B	N									
ATOM	2195	C	LYS	B	162	29.933	32.208	19.910	1.00	12.51
B	C									
ATOM	2196	O	LYS	B	162	29.445	31.442	19.078	1.00	13.34
B	O									
ATOM	2197	N	ALA	B	163	30.611	33.297	19.574	1.00	12.30
B	N									
ATOM	2198	CA	ALA	B	163	30.822	33.656	18.177	1.00	12.59
B	C									
ATOM	2199	CB	ALA	B	163	31.474	35.036	18.089	1.00	12.94
B	C									
ATOM	2200	C	ALA	B	163	31.684	32.617	17.454	1.00	12.63
B	C									

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ATOM	2201	O	ALA B 163	31.435	32.281	16.293	1.00	13.56
B	O							
ATOM	2202	N	ILE B 164	32.704	32.111	18.135	1.00	13.23
B	N							
ATOM	2203	CA	ILE B 164	33.578	31.107	17.532	1.00	10.59
B	C							
ATOM	2204	CB	ILE B 164	34.824	30.853	18.403	1.00	12.38
B	C							
ATOM	2205	CG2	ILE B 164	35.701	29.767	17.768	1.00	8.98
B	C							
ATOM	2206	CG1	ILE B 164	35.617	32.155	18.566	1.00	9.24
B	C							
ATOM	2207	CD	ILE B 164	36.746	32.058	19.590	1.00	11.68
B	C							
ATOM	2208	C	ILE B 164	32.793	29.804	17.379	1.00	12.14
B	C							
ATOM	2209	O	ILE B 164	33.009	29.049	16.431	1.00	12.85
B	O							
ATOM	2210	N	GLY B 165	31.868	29.558	18.305	1.00	10.88
B	N							
ATOM	2211	CA	GLY B 165	31.063	28.345	18.252	1.00	13.41
B	C							
ATOM	2212	C	GLY B 165	30.109	28.337	17.072	1.00	14.68
B	C							
ATOM	2213	O	GLY B 165	29.583	27.290	16.686	1.00	14.73
B	O							
ATOM	2214	N	GLU B 166	29.890	29.512	16.495	1.00	13.01
B	N							
ATOM	2215	CA	GLU B 166	29.011	29.656	15.349	1.00	14.06
B	C							
ATOM	2216	CB	GLU B 166	28.031	30.773	15.621	1.00	16.63
B	C							
ATOM	2217	CG	GLU B 166	27.344	30.594	16.942	1.00	21.35
B	C							
ATOM	2218	CD	GLU B 166	26.278	29.510	16.908	1.00	25.81
B	C							
ATOM	2219	OE1	GLU B 166	26.648	28.326	16.873	1.00	31.72
B	O							
ATOM	2220	OE2	GLU B 166	25.065	29.822	16.913	1.00	30.04
B	O							
ATOM	2221	C	GLU B 166	29.767	29.952	14.062	1.00	11.84
B	C							
ATOM	2222	O	GLU B 166	29.164	30.323	13.054	1.00	11.51
B	O							
ATOM	2223	N	LEU B 167	31.084	29.781	14.090	1.00	10.92
B	N							
ATOM	2224	CA	LEU B 167	31.895	30.033	12.903	1.00	12.37
B	C							
ATOM	2225	CB	LEU B 167	33.391	29.836	13.195	1.00	15.29
B	C							
ATOM	2226	CG	LEU B 167	34.115	31.001	13.872	1.00	20.06
B	C							
ATOM	2227	CD1	LEU B 167	35.562	30.612	14.125	1.00	22.06
B	C							
ATOM	2228	CD2	LEU B 167	34.033	32.247	12.996	1.00	20.29
B	C							
ATOM	2229	C	LEU B 167	31.496	29.137	11.739	1.00	13.10
B	C							

ATOM	2230	O	LEU B 167	31.733	29.481	10.585	1.00	12.57
B	O							
ATOM	2231	N	ASP B 168	30.901	27.986	12.034	1.00	12.74
B	N							
ATOM	2232	CA	ASP B 168	30.478	27.100	10.960	1.00	14.28
B	C							
ATOM	2233	CB	ASP B 168	30.058	25.727	11.515	1.00	13.57
B	C							
ATOM	2234	CG	ASP B 168	29.185	25.821	12.760	1.00	17.07
B	C							
ATOM	2235	OD1	ASP B 168	28.964	26.930	13.295	1.00	14.89
B	O							
ATOM	2236	OD2	ASP B 168	28.723	24.755	13.218	1.00	18.76
B	O							
ATOM	2237	C	ASP B 168	29.335	27.767	10.186	1.00	12.65
B	C							
ATOM	2238	O	ASP B 168	29.312	27.747	8.958	1.00	13.63
B	O							
ATOM	2239	N	LEU B 169	28.403	28.379	10.903	1.00	11.65
B	N							
ATOM	2240	CA	LEU B 169	27.293	29.068	10.255	1.00	14.38
B	C							
ATOM	2241	CB	LEU B 169	26.245	29.481	11.283	1.00	15.94
B	C							
ATOM	2242	CG	LEU B 169	25.462	28.363	11.971	1.00	18.22
B	C							
ATOM	2243	CD1	LEU B 169	24.391	28.973	12.880	1.00	18.16
B	C							
ATOM	2244	CD2	LEU B 169	24.822	27.472	10.913	1.00	20.52
B	C							
ATOM	2245	C	LEU B 169	27.791	30.311	9.520	1.00	15.25
B	C							
ATOM	2246	O	LEU B 169	27.249	30.701	8.483	1.00	14.55
B	O							
ATOM	2247	N	LEU B 170	28.821	30.944	10.062	1.00	15.29
B	N							
ATOM	2248	CA	LEU B 170	29.359	32.133	9.421	1.00	16.17
B	C							
ATOM	2249	CB	LEU B 170	30.418	32.795	10.309	1.00	16.47
B	C							
ATOM	2250	CG	LEU B 170	31.234	33.908	9.639	1.00	18.75
B	C							
ATOM	2251	CD1	LEU B 170	30.309	34.997	9.152	1.00	20.23
B	C							
ATOM	2252	CD2	LEU B 170	32.242	34.479	10.622	1.00	20.78
B	C							
ATOM	2253	C	LEU B 170	29.976	31.742	8.088	1.00	16.04
B	C							
ATOM	2254	O	LEU B 170	29.754	32.397	7.069	1.00	17.27
B	O							
ATOM	2255	N	PHE B 171	30.748	30.663	8.104	1.00	15.59
B	N							
ATOM	2256	CA	PHE B 171	31.418	30.173	6.905	1.00	17.71
B	C							
ATOM	2257	CB	PHE B 171	32.313	28.978	7.271	1.00	18.23
B	C							
ATOM	2258	CG	PHE B 171	33.023	28.355	6.093	1.00	23.19
B	C							

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ATOM	2259	CD1	PHE	B	171	32.324	27.606	5.147	1.00	25.08
B	C									
ATOM	2260	CD2	PHE	B	171	34.395	28.521	5.930	1.00	25.84
B	C									
ATOM	2261	CE1	PHE	B	171	32.982	27.031	4.053	1.00	26.30
B	C									
ATOM	2262	CE2	PHE	B	171	35.064	27.949	4.840	1.00	26.12
B	C									
ATOM	2263	CZ	PHE	B	171	34.353	27.204	3.902	1.00	25.36
B	C									
ATOM	2264	C	PHE	B	171	30.413	29.773	5.824	1.00	15.84
B	C									
ATOM	2265	O	PHE	B	171	30.545	30.158	4.657	1.00	15.02
B	O									
ATOM	2266	N	MET	B	172	29.411	28.991	6.207	1.00	15.66
B	N									
ATOM	2267	CA	MET	B	172	28.407	28.548	5.241	1.00	14.21
B	C									
ATOM	2268	CB	MET	B	172	27.505	27.484	5.859	1.00	14.82
B	C									
ATOM	2269	CG	MET	B	172	28.167	26.139	6.076	1.00	17.32
B	C									
ATOM	2270	SD	MET	B	172	28.576	25.335	4.523	1.00	19.02
B	S									
ATOM	2271	CE	MET	B	172	30.140	24.649	4.909	1.00	18.35
B	C									
ATOM	2272	C	MET	B	172	27.552	29.701	4.723	1.00	15.52
B	C									
ATOM	2273	O	MET	B	172	27.216	29.750	3.543	1.00	16.04
B	O									
ATOM	2274	N	SER	B	173	27.191	30.623	5.610	1.00	17.55
B	N									
ATOM	2275	CA	SER	B	173	26.368	31.766	5.225	1.00	19.47
B	C									
ATOM	2276	CB	SER	B	173	25.962	32.554	6.462	1.00	18.60
B	C									
ATOM	2277	OG	SER	B	173	25.085	31.797	7.272	1.00	20.37
B	O									
ATOM	2278	C	SER	B	173	27.123	32.671	4.262	1.00	21.94
B	C									
ATOM	2279	O	SER	B	173	26.551	33.201	3.303	1.00	22.14
B	O									
ATOM	2280	N	LEU	B	174	28.412	32.853	4.523	1.00	22.66
B	N									
ATOM	2281	CA	LEU	B	174	29.252	33.688	3.676	1.00	23.53
B	C									
ATOM	2282	CB	ALEU	B	174	30.652	33.804	4.287	0.50	23.45
B	C									
ATOM	2283	CB	BLEU	B	174	30.671	33.756	4.215	0.50	23.44
B	C									
ATOM	2284	CG	ALEU	B	174	31.647	34.741	3.608	0.50	23.66
B	C									
ATOM	2285	CG	BLEU	B	174	31.036	34.904	5.148	0.50	23.44
B	C									
ATOM	2286	CD1	ALEU	B	174	31.128	36.165	3.669	0.50	23.07
B	C									
ATOM	2287	CD1	BLEU	B	174	32.414	34.656	5.737	0.50	22.70
B	C									

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ATOM	2288	CD2ALEU	B	174	32.995	34.633	4.308	0.50	22.85
B	C								
ATOM	2289	CD2BLEU	B	174	31.012	36.205	4.367	0.50	23.54
B	C								
ATOM	2290	C	LEU	B 174	29.340	33.097	2.274	1.00	25.13
B	C								
ATOM	2291	O	LEU	B 174	29.225	33.814	1.282	1.00	25.73
B	O								
ATOM	2292	N	ARG	B 175	29.547	31.785	2.204	1.00	25.47
B	N								
ATOM	2293	CA	ARG	B 175	29.641	31.074	0.933	1.00	26.85
B	C								
ATOM	2294	CB	ARG	B 175	29.872	29.584	1.196	1.00	28.61
B	C								
ATOM	2295	CG	ARG	B 175	30.384	28.818	0.006	1.00	31.65
B	C								
ATOM	2296	CD	ARG	B 175	30.369	27.331	0.279	1.00	35.80
B	C								
ATOM	2297	NE	ARG	B 175	29.017	26.786	0.193	1.00	37.83
B	N								
ATOM	2298	CZ	ARG	B 175	28.317	26.731	-0.935	1.00	41.57
B	C								
ATOM	2299	NH1	ARG	B 175	28.849	27.183	-2.060	1.00	42.90
B	N								
ATOM	2300	NH2	ARG	B 175	27.084	26.238	-0.944	1.00	42.15
B	N								
ATOM	2301	C	ARG	B 175	28.365	31.264	0.101	1.00	26.48
B	C								
ATOM	2302	O	ARG	B 175	28.416	31.705	-1.049	1.00	27.29
B	O								
ATOM	2303	N	ASN	B 176	27.216	30.954	0.690	1.00	24.26
B	N								
ATOM	2304	CA	ASN	B 176	25.943	31.095	-0.010	1.00	25.29
B	C								
ATOM	2305	CB	ASN	B 176	24.831	30.435	0.798	1.00	22.74
B	C								
ATOM	2306	CG	ASN	B 176	24.682	28.972	0.469	1.00	24.13
B	C								
ATOM	2307	OD1	ASN	B 176	25.668	28.285	0.187	1.00	22.83
B	O								
ATOM	2308	ND2	ASN	B 176	23.447	28.479	0.503	1.00	20.65
B	N								
ATOM	2309	C	ASN	B 176	25.539	32.522	-0.348	1.00	26.76
B	C								
ATOM	2310	O	ASN	B 176	24.759	32.753	-1.276	1.00	26.72
B	O								
ATOM	2311	N	ALA	B 177	26.068	33.481	0.397	1.00	25.95
B	N								
ATOM	2312	CA	ALA	B 177	25.729	34.870	0.162	1.00	26.17
B	C								
ATOM	2313	CB	ALA	B 177	25.737	35.633	1.487	1.00	24.10
B	C								
ATOM	2314	C	ALA	B 177	26.663	35.550	-0.826	1.00	25.49
B	C								
ATOM	2315	O	ALA	B 177	26.275	36.511	-1.478	1.00	25.51
B	O								
ATOM	2316	N	CYS	B 178	27.879	35.033	-0.964	1.00	27.87
B	N								

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ATOM	2317	CA	CYS B 178	28.862	35.671	-1.820	1.00	27.66
B	C							
ATOM	2318	C	CYS B 178	29.271	34.977	-3.128	1.00	29.33
B	C							
ATOM	2319	O	CYS B 178	29.732	35.666	-4.035	1.00	31.34
B	O							
ATOM	2320	CB	CYS B 178	30.123	35.902	-0.991	1.00	27.05
B	C							
ATOM	2321	SG	CYS B 178	29.912	37.031	0.419	1.00	25.07
B	S							
ATOM	2322	N	ILE B 179	29.109	33.664	-3.245	1.00	30.95
B	N							
ATOM	2323	CA	ILE B 179	29.490	33.008	-4.491	1.00	31.56
B	C							
ATOM	2324	CB	ILE B 179	29.681	31.496	-4.309	1.00	32.47
B	C							
ATOM	2325	CG2	ILE B 179	30.764	31.239	-3.275	1.00	34.45
B	C							
ATOM	2326	CG1	ILE B 179	28.356	30.851	-3.899	1.00	33.65
B	C							
ATOM	2327	CD	ILE B 179	28.408	29.343	-3.849	1.00	35.23
B	C							
ATOM	2328	C	ILE B 179	28.441	33.220	-5.576	1.00	31.05
B	C							
ATOM	2329	OT1	ILE B 179	27.279	33.539	-5.240	1.00	29.84
B	O							
ATOM	2330	OT2	ILE B 179	28.806	33.043	-6.756	1.00	32.57
B	O							
HETATM	2331	O	HOH W 201	27.297	23.446	24.432	1.00	10.44
W	O							
HETATM	2332	O	HOH W 202	29.001	24.489	16.199	1.00	15.87
W	O							
HETATM	2333	O	HOH W 203	11.736	25.818	21.510	1.00	19.00
W	O							
HETATM	2334	O	HOH W 204	24.143	15.462	11.058	1.00	16.00
W	O							
HETATM	2335	O	HOH W 205	13.986	10.421	2.897	1.00	47.98
W	O							
HETATM	2336	O	HOH W 206	9.264	23.783	21.316	1.00	19.55
W	O							
HETATM	2337	O	HOH W 207	26.417	26.497	21.231	1.00	16.89
W	O							
HETATM	2338	O	HOH W 208	25.199	18.812	10.440	1.00	16.53
W	O							
HETATM	2339	O	HOH W 209	27.671	14.819	7.534	1.00	15.58
W	O							
HETATM	2340	O	HOH W 210	17.220	31.319	12.529	1.00	18.46
W	O							
HETATM	2341	O	HOH W 211	7.763	15.191	13.315	1.00	16.34
W	O							
HETATM	2342	O	HOH W 212	25.429	52.025	16.393	1.00	21.97
W	O							
HETATM	2343	O	HOH W 213	4.366	14.026	-0.146	1.00	16.43
W	O							
HETATM	2344	O	HOH W 214	30.378	15.252	8.290	1.00	17.71
W	O							
HETATM	2345	O	HOH W 215	29.716	36.103	14.680	1.00	26.32
W	O							

HETATM	2346	O	HOH W 216	29.851	44.950	27.330	1.00	16.23
W	O							
HETATM	2347	O	HOH W 217	25.965	42.188	-1.336	1.00	26.70
W	O							
HETATM	2348	O	HOH W 218	32.742	40.348	23.501	1.00	19.93
W	O							
HETATM	2349	O	HOH W 219	21.669	14.477	11.866	1.00	21.69
W	O							
HETATM	2350	O	HOH W 220	34.189	40.928	21.191	1.00	21.11
W	O							
HETATM	2351	O	HOH W 221	13.503	33.656	-0.622	1.00	21.91
W	O							
HETATM	2352	O	HOH W 222	24.529	39.089	-2.108	1.00	22.69
W	O							
HETATM	2353	O	HOH W 223	20.087	30.335	-0.404	1.00	26.82
W	O							
HETATM	2354	O	HOH W 224	21.910	37.842	18.502	1.00	21.17
W	O							
HETATM	2355	O	HOH W 225	19.543	26.452	-10.389	1.00	24.04
W	O							
HETATM	2356	O	HOH W 226	15.561	31.685	14.681	1.00	45.81
W	O							
HETATM	2357	O	HOH W 227	32.308	36.045	30.019	1.00	28.38
W	O							
HETATM	2358	O	HOH W 228	17.729	31.816	1.688	1.00	18.99
W	O							
HETATM	2359	O	HOH W 229	25.158	23.427	25.705	1.00	23.41
W	O							
HETATM	2360	O	HOH W 230	27.991	29.102	19.752	1.00	20.66
W	O							
HETATM	2361	O	HOH W 231	3.725	18.194	12.154	1.00	33.73
W	O							
HETATM	2362	O	HOH W 232	37.621	42.067	21.510	1.00	27.85
W	O							
HETATM	2363	O	HOH W 233	19.597	28.257	20.861	1.00	28.65
W	O							
HETATM	2364	O	HOH W 234	20.056	40.743	13.648	1.00	32.86
W	O							
HETATM	2365	O	HOH W 235	11.670	39.187	7.650	1.00	30.82
W	O							
HETATM	2366	O	HOH W 236	18.418	33.049	20.243	1.00	26.85
W	O							
HETATM	2367	O	HOH W 237	23.466	27.862	16.542	1.00	25.38
W	O							
HETATM	2368	O	HOH W 238	36.544	43.733	3.953	1.00	24.65
W	O							
HETATM	2369	O	HOH W 239	20.855	44.986	20.266	1.00	20.67
W	O							
HETATM	2370	O	HOH W 240	6.104	33.041	6.261	1.00	34.43
W	O							
HETATM	2371	O	HOH W 241	22.194	38.315	15.523	1.00	30.42
W	O							
HETATM	2372	O	HOH W 242	26.322	47.696	12.361	1.00	28.82
W	O							
HETATM	2373	O	HOH W 243	29.634	17.921	1.255	1.00	23.78
W	O							
HETATM	2374	O	HOH W 244	12.805	39.529	5.415	1.00	48.81
W	O							



HETATM	2375	O	HOH W 245	9.624	26.277	4.198	1.00	24.30
W	O							
HETATM	2376	O	HOH W 246	7.395	13.510	7.017	1.00	35.04
W	O							
HETATM	2377	O	HOH W 247	30.410	33.686	14.273	1.00	21.60
W	O							
HETATM	2378	O	HOH W 248	36.748	43.355	23.420	1.00	28.82
W	O							
HETATM	2379	O	HOH W 249	19.550	13.720	10.528	1.00	21.91
W	O							
HETATM	2380	O	HOH W 250	17.891	27.372	-12.427	1.00	32.70
W	O							
HETATM	2381	O	HOH W 251	31.614	45.127	10.612	1.00	28.57
W	O							
HETATM	2382	O	HOH W 252	36.318	24.599	24.398	1.00	27.35
W	O							
HETATM	2383	O	HOH W 253	27.851	21.966	22.159	1.00	35.57
W	O							
HETATM	2384	O	HOH W 254	12.195	26.188	3.549	1.00	21.42
W	O							
HETATM	2385	O	HOH W 255	14.952	35.943	7.315	1.00	31.47
W	O							
HETATM	2386	O	HOH W 256	25.476	31.892	15.021	1.00	42.15
W	O							
HETATM	2387	O	HOH W 257	33.419	16.973	5.504	1.00	24.87
W	O							
HETATM	2388	O	HOH W 258	2.676	21.388	9.316	1.00	35.75
W	O							
HETATM	2389	O	HOH W 259	25.575	34.428	-3.222	1.00	39.98
W	O							
HETATM	2390	O	HOH W 260	14.941	30.863	-2.385	1.00	26.04
W	O							
HETATM	2391	O	HOH W 261	41.672	27.415	23.709	1.00	35.93
W	O							
HETATM	2392	O	HOH W 262	18.136	30.604	21.993	1.00	31.10
W	O							
HETATM	2393	O	HOH W 263	32.907	42.731	25.674	1.00	26.77
W	O							
HETATM	2394	O	HOH W 264	21.328	33.022	-5.079	1.00	32.93
W	O							
HETATM	2395	O	HOH W 265	28.052	12.336	6.540	1.00	22.14
W	O							
HETATM	2396	O	HOH W 266	2.099	19.008	5.021	1.00	32.55
W	O							
HETATM	2397	O	HOH W 267	29.794	31.341	25.289	1.00	32.81
W	O							
HETATM	2398	O	HOH W 268	20.757	45.357	22.862	1.00	36.33
W	O							
HETATM	2399	O	HOH W 269	18.249	16.829	-10.961	1.00	31.63
W	O							
HETATM	2400	O	HOH W 270	5.371	13.454	-3.003	1.00	38.53
W	O							
HETATM	2401	O	HOH W 271	29.440	31.283	29.531	1.00	42.43
W	O							
HETATM	2402	O	HOH W 272	28.073	49.822	16.597	1.00	34.43
W	O							
HETATM	2403	O	HOH W 273	9.569	37.651	14.685	1.00	41.67
W	O							

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HETATM	2404	O	HOH W 274	3.582	23.223	-3.241	1.00	41.20
W	O							
HETATM	2405	O	HOH W 275	39.303	37.931	25.088	1.00	35.26
W	O							
HETATM	2406	O	HOH W 276	27.169	49.230	14.079	1.00	27.21
W	O							
HETATM	2407	O	HOH W 277	17.385	35.595	-7.830	1.00	39.15
W	O							
HETATM	2408	O	HOH W 278	36.093	19.433	19.171	1.00	57.03
W	O							
HETATM	2409	O	HOH W 279	31.185	14.743	10.858	1.00	33.84
W	O							
HETATM	2410	O	HOH W 280	16.886	31.999	-1.178	1.00	30.74
W	O							
HETATM	2411	O	HOH W 281	23.320	12.684	6.853	1.00	38.74
W	O							
HETATM	2412	O	HOH W 282	35.109	41.222	24.391	1.00	35.21
W	O							
HETATM	2413	O	HOH W 283	43.171	19.919	0.844	1.00	31.45
W	O							
HETATM	2414	O	HOH W 284	21.356	14.695	23.557	1.00	28.47
W	O							
HETATM	2415	O	HOH W 285	24.661	10.570	6.602	1.00	45.63
W	O							
HETATM	2416	O	HOH W 286	4.247	12.050	1.832	1.00	39.46
W	O							
HETATM	2417	O	HOH W 287	40.280	39.948	24.240	1.00	33.27
W	O							
HETATM	2418	O	HOH W 288	20.284	56.897	0.611	1.00	44.29
W	O							
HETATM	2419	O	HOH W 289	23.310	31.108	15.564	1.00	38.31
W	O							
HETATM	2420	O	HOH W 290	48.053	26.077	15.288	1.00	47.19
W	O							
HETATM	2421	O	HOH W 291	12.020	16.304	20.731	1.00	28.99
W	O							
HETATM	2422	O	HOH W 292	41.231	23.934	2.570	1.00	33.94
W	O							
HETATM	2423	O	HOH W 293	18.669	11.706	-13.630	1.00	36.09
W	O							
HETATM	2424	O	HOH W 294	8.109	34.730	7.563	1.00	39.26
W	O							
HETATM	2425	O	HOH W 295	15.600	35.689	-4.228	1.00	41.15
W	O							
HETATM	2426	O	HOH W 296	-4.142	24.573	20.605	1.00	42.87
W	O							
HETATM	2427	O	HOH W 297	15.622	34.076	15.219	1.00	42.95
W	O							
HETATM	2428	O	HOH W 298	38.169	40.792	23.402	1.00	45.01
W	O							
HETATM	2429	O	HOH W 299	27.537	26.052	-3.736	1.00	52.95
W	O							
HETATM	2430	O	HOH W 300	35.494	16.860	10.304	1.00	43.09
W	O							
HETATM	2431	O	HOH W 301	41.551	21.663	1.380	1.00	36.94
W	O							
HETATM	2432	O	HOH W 302	45.225	29.031	6.035	1.00	40.03
W	O							

HETATM	2433	O	HOH W 303	31.772	47.636	4.279	1.00	35.07
W	O							
HETATM	2434	O	HOH W 304	16.888	20.002	-11.152	1.00	39.19
W	O							
HETATM	2435	O	HOH W 305	15.036	31.029	17.354	1.00	42.31
W	O							
HETATM	2436	O	HOH W 306	8.035	38.484	2.278	1.00	36.39
W	O							
HETATM	2437	O	HOH W 307	7.021	9.870	24.009	1.00	46.58
W	O							
HETATM	2438	O	HOH W 308	-0.328	27.092	-6.529	1.00	39.32
W	O							
HETATM	2439	O	HOH W 309	32.290	44.882	-6.224	1.00	41.91
W	O							
HETATM	2440	O	HOH W 310	-2.886	27.829	1.400	1.00	46.46
W	O							
HETATM	2441	O	HOH W 311	45.080	21.111	1.259	1.00	43.31
W	O							
HETATM	2442	O	HOH W 312	34.187	18.021	11.951	1.00	33.37
W	O							
HETATM	2443	O	HOH W 313	42.013	42.835	15.912	1.00	35.29
W	O							
HETATM	2444	O	HOH W 314	21.506	9.309	4.752	1.00	35.56
W	O							
HETATM	2445	O	HOH W 315	33.745	38.255	30.145	1.00	42.37
W	O							
HETATM	2446	O	HOH W 316	26.849	28.079	-7.783	1.00	42.24
W	O							
HETATM	2447	O	HOH W 317	22.190	18.955	-5.896	1.00	44.87
W	O							
HETATM	2448	O	HOH W 318	5.056	11.251	-3.217	1.00	43.78
W	O							
HETATM	2449	O	HOH W 319	30.465	47.010	-8.187	1.00	60.12
W	O							
HETATM	2450	O	HOH W 320	25.131	34.069	-7.705	1.00	40.30
W	O							
HETATM	2451	O	HOH W 321	-1.120	23.587	2.285	1.00	57.54
W	O							
HETATM	2452	O	HOH W 322	27.796	32.147	25.994	1.00	52.28
W	O							
HETATM	2453	O	HOH W 323	2.796	19.619	-4.238	1.00	43.84
W	O							
HETATM	2454	O	HOH W 324	4.253	33.074	8.597	1.00	38.14
W	O							
HETATM	2455	O	HOH W 325	28.162	22.354	26.470	1.00	46.35
W	O							
HETATM	2456	O	HOH W 326	17.658	41.562	-4.831	1.00	45.26
W	O							
HETATM	2457	O	HOH W 327	12.525	24.278	23.101	1.00	49.33
W	O							
HETATM	2458	O	HOH W 328	1.417	20.936	21.185	1.00	51.98
W	O							
HETATM	2459	O	HOH W 329	5.110	34.325	4.685	1.00	47.55
W	O							
HETATM	2460	O	HOH W 330	23.854	24.173	-8.875	1.00	53.09
W	O							
HETATM	2461	O	HOH W 331	26.863	30.894	27.666	1.00	47.65
W	O							

HETATM	2462	O	HOH W 332	32.534	14.831	7.143	1.00	39.84
W	O							
HETATM	2463	O	HOH W 333	15.358	12.945	-2.666	1.00	37.81
W	O							
HETATM	2464	O	HOH W 334	44.680	33.725	22.138	1.00	49.77
W	O							
HETATM	2465	O	HOH W 335	12.020	38.120	13.522	1.00	58.79
W	O							
HETATM	2466	O	HOH W 336	42.127	30.661	-3.910	1.00	44.39
W	O							
HETATM	2467	O	HOH W 337	1.727	20.705	6.878	1.00	45.75
W	O							
HETATM	2468	O	HOH W 338	-0.384	35.128	-7.818	1.00	49.01
W	O							
HETATM	2469	O	HOH W 339	21.057	43.781	28.030	1.00	40.90
W	O							
HETATM	2470	O	HOH W 340	11.861	9.923	3.834	1.00	41.37
W	O							
HETATM	2471	O	HOH W 341	37.937	37.279	28.479	1.00	59.04
W	O							
HETATM	2472	O	HOH W 342	6.363	12.922	12.257	1.00	43.48
W	O							
HETATM	2473	O	HOH W 343	2.799	32.430	24.168	1.00	60.02
W	O							
HETATM	2474	O	HOH W 344	29.796	50.785	1.614	1.00	53.08
W	O							
HETATM	2475	O	HOH W 345	-0.874	32.698	-7.319	1.00	39.33
W	O							
HETATM	2476	O	HOH W 346	36.654	46.102	-3.751	1.00	49.64
W	O							
HETATM	2477	O	HOH W 347	22.253	20.580	21.775	1.00	38.38
W	O							
HETATM	2478	O	HOH W 348	23.536	39.353	28.221	1.00	50.03
W	O							
HETATM	2479	O	HOH W 349	21.979	23.483	27.337	1.00	56.78
W	O							
HETATM	2480	O	HOH W 350	15.688	9.390	6.304	1.00	39.68
W	O							
HETATM	2481	O	HOH W 351	17.446	31.911	24.017	1.00	49.08
W	O							
HETATM	2482	O	HOH W 352	20.424	32.203	-1.926	1.00	52.71
W	O							
HETATM	2483	O	HOH W 353	7.374	38.066	19.040	1.00	52.43
W	O							
HETATM	2484	O	HOH W 354	40.616	34.974	29.409	1.00	43.05
W	O							
HETATM	2485	O	HOH W 355	13.964	28.600	20.763	1.00	45.36
W	O							
HETATM	2486	O	HOH W 356	21.968	11.935	4.239	1.00	34.43
W	O							
HETATM	2487	O	HOH W 357	40.741	40.054	-5.266	1.00	50.01
W	O							
HETATM	2488	O	HOH W 358	1.011	22.226	10.873	1.00	47.98
W	O							
HETATM	2489	O	HOH W 359	30.521	24.949	-3.484	1.00	51.24
W	O							
HETATM	2490	O	HOH W 360	30.394	22.663	13.867	1.00	35.80
W	O							

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HETATM	2491	O	HOH W 361	1.298	28.757	23.599	1.00	45.73
W	O							
HETATM	2492	O	HOH W 362	10.037	16.429	-9.605	1.00	43.70
W	O							
HETATM	2493	O	HOH W 363	2.342	16.995	19.296	1.00	53.29
W	O							
HETATM	2494	O	HOH W 364	18.754	21.800	-12.588	1.00	56.18
W	O							
HETATM	2495	O	HOH W 365	18.388	23.021	28.255	1.00	48.80
W	O							
HETATM	2496	O	HOH W 366	12.812	40.928	2.593	1.00	50.81
W	O							
HETATM	2497	O	HOH W 367	20.573	19.834	-9.838	1.00	49.46
W	O							
HETATM	2498	O	HOH W 368	3.924	11.192	4.654	1.00	47.96
W	O							
HETATM	2499	O	HOH W 369	23.969	20.116	-9.041	1.00	44.24
W	O							
HETATM	2500	O	HOH W 370	40.480	32.964	1.998	1.00	52.22
W	O							
HETATM	2501	O	HOH W 371	20.730	46.882	18.743	1.00	38.87
W	O							
HETATM	2502	O	HOH W 372	29.891	46.902	11.620	1.00	41.85
W	O							
HETATM	2503	O	HOH W 373	27.107	45.779	-9.724	1.00	49.81
W	O							
HETATM	2504	O	HOH W 374	45.521	35.688	5.405	1.00	50.64
W	O							
HETATM	2505	O	HOH W 375	8.631	12.370	10.753	1.00	41.87
W	O							
HETATM	2506	O	HOH W 376	-1.414	24.184	8.066	1.00	45.18
W	O							
HETATM	2507	O	HOH W 377	25.847	26.771	-9.623	1.00	50.58
W	O							
HETATM	2508	O	HOH W 378	17.044	35.686	20.995	1.00	46.08
W	O							
HETATM	2509	O	HOH W 379	31.859	30.020	27.009	1.00	44.41
W	O							
HETATM	2510	O	HOH W 380	15.331	35.172	17.686	1.00	42.80
W	O							
HETATM	2511	O	HOH W 381	30.163	27.844	-12.299	1.00	48.94
W	O							
HETATM	2512	O	HOH W 382	26.459	20.674	25.974	1.00	50.90
W	O							
HETATM	2513	O	HOH W 383	11.215	40.705	-7.869	1.00	44.77
W	O							
HETATM	2514	O	HOH W 384	39.653	28.993	25.532	1.00	42.77
W	O							
HETATM	2515	O	HOH W 385	8.320	22.025	23.135	1.00	40.98
W	O							
HETATM	2516	O	HOH W 386	19.109	57.899	2.281	1.00	52.58
W	O							
HETATM	2517	O	HOH W 387	23.211	31.034	3.809	0.68	12.76
W	O							
HETATM	2518	O	HOH W 388	23.669	33.864	2.886	0.68	17.24
W	O							
HETATM	2519	O	HOH W 389	22.013	32.823	3.876	0.68	32.76
W	O							

END

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<sup>†</sup>Amino acid residues correspond to residues in human IL-22, SEQ ID NO: 2.

25114717.1

Table 5: Solvent exposed residues of hIL-22.<sup>1</sup>

Residue	Solvent Exposed Area (Å <sup>2</sup> ) <sup>2</sup>	Residue	Solvent Exposed Area (Å <sup>2</sup> )
SER38	80.00	HIS39	131.00
ARG41	112.00	ASP43	91.00
LYS44	82.00	SER45	49.00
ASN46	46.00	GLN48	103.00
GLN49	91.00	PRO50	99.00
TYR51	124.00	ILE52	24.00
THR53	27.00	ASN54	81.00
ARG55	51.00	PHE57	69.00
MET58	51.00	LYS61	123.00
GLU62	70.00	SER64	42.00
LEU65	135.00	ALA66	53.00
ASP67	27.00	ASN68	141.00
ASN69	35.00	THR70	126.00
ASP71	142.00	VAL72	45.00
ARG73	141.00	LEU74	11.00
ILE75	18.00	GLY76	13.00
GLU77	159.00	LYS78	116.00
PHE80	39.00	HIS81	141.00
GLY82	60.00	SER84	49.00
MET85	131.00	SER86	103.00
GLU87	22.00	ARG88	53.00
TYR90	31.00	LYS93	20.00
GLN94	49.00	ASN97	40.00
PHE98	10.00	GLU101	113.00
GLU102	83.00	PHE105	86.00
PRO106	72.00	SER108	46.00
ASP109	113.00	ARG110	96.00
PHE111	23.00	GLN112	136.00
PRO113	78.00	TYR114	54.00
GLN116	79.00	GLU117	60.00
VAL119	16.00	PRO120	58.00
PHE121	13.00	ALA123	33.00
ARG124	157.00	LEU125	3.00
SER126	20.00	ASN127	114.00
ARG128	126.00	SER130	54.00
THR131	117.00	HIS133	105.00
ILE134	30.00	GLU135	195.00
GLY136	39.00	ASP137	102.00
ASP138	39.00	LEU139	73.00
HIS140	48.00	GLN142	115.00
ARG143	155.00	ASN144	27.00
GLN146	80.00	LYS147	109.00

LYS149 53.00

ASP150

53.00

**Table 5: Continued<sup>1</sup>**

<b>Residue</b>	<b>Solvent Exposed Area (Å<sup>2</sup>)<sup>2</sup></b>	<b>Residue</b>	<b>Solvent Exposed Area (Å<sup>2</sup>)</b>
THR151	21.00	LYS153	127.00
LYS154	147.00	LEU155	37.00
GLY156	29.00	GLU157	104.00
SER158	32.00	GLU160	35.00
ILE161	11.00	LYS162	6.00
ALA163	11.00	GLY165	11.00
GLU166	15.00	ASP168	40.00
LEU169	38.00	MET172	86.00
SER173	15.00	ARG175	70.00
ASN176	112.00	ALA177	21.00
ILE179	89.00		

Total area of chain A: 7584.

<sup>1</sup> Amino acid residues correspond to residues in human IL-22, SEQ ID NO: 2.<sup>2</sup> Solvent exposed areas c